Figure 1

VSGGSINSGDYYWSWIRQHPGKGLDCIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFFLKLTSVTAADTAVYYCARSTVVNPGWFDPWGQGTLVTVSS (SEQ ID NO:3)

CDR1 CDR2 CDR3

Figure 2

GTCTCTGGTG GCTCCATCAA CAGTGGTGAT TACTACTGGA GCTGGATCCG CCAGCACCCA GGGAAGGGCC TGGACTGCAT TGGGTACATC TATTACAGTG GGAGCACCTA
CTACAACCCG TCCCTCAAGA GTCGAGTTAC CATATCAGTA GACACGTCTA AGAATCAGTT CTTCCTGAAG CTGACCTCTG TGACTGCCGC GGACACGGCC GTGTATTACT
GTGCGAGATC TACGGTGGTA AATCCGGGGT GGTTCGACCC CTGGGGCCAR GGAACCCTGG TCACCGTCTC CTCA (SEQ ID NO:4) 3

Figure 3

TITCQASQDINNYLNWFQQKPGKAPKVLIHDASNLETGGPSRFSGSGSGTDFTFTISGLQPEDIATYYCQQYESLPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQ (SEQ ID NO:5) 24

CDR1 CDR2 CDR3

Figure 4

ACCATCACTT GCCAGGCGAG TCAGGACATT AACAACTATT TAAATTGGTT TCAGCAGAAA CCAGGGAAAG CCCCT AAGGTCCTGA TCCACGATGC ATCCAATTTG
GAAACAGGGG GCCCATCAAG GTTCAGTGGA AGTGGATCTG GGACA GATTTTACTT TCACCATCAG CGGCCTGCAG CCTGAAGACA TTGCAACATA TTATTGTCAA
CAGTATGAAA GTCTC CCACTCACTT TCGGCGGAGG GACCAAGGTG GAGATCAAA (SEQ ID NO:6) 4

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Figure 5

VSGGSINSGDYYWSWIRQHPGKGLEWIGSIYYSGNTFYNPSLKSRVTISLDTSKNQFSLKLSSVTAADTAVCYCARNIVTTGAFDIWGQGTMVTVSS (SEQ ID NO:7) 25

CDR1 CDR2 CDR3

Figure 6

GTCTCTGGTG GCTCCATCAA CAGTGGTGAT TACTACTGGA GCTGGATCCG CCAGCACCCA GGGAAGGGCC TGGAGTGGAT TGGGTCCATC TATTACAGTG GGAACACCTT
CTACAACCCG TCCCTCAAGA GTCGAGTTAC CATATCACTA GACACGTCTA AGAACCAGTT CTCCCTGAAG CTGAGTTCTG TGACTGCCGC GGACACGGCC GTGTGTTACT
GTGCGAGAAA TATAGTGACT ACGGGTGCTT TTGATATCTG GGGCCAAGGG ACAATGGTCA CCGTCTCTTC A (SEQ ID NO:8) 5

Figure 7

TITCQASQDITIYLNWYQQKPGKAPKLLINDASSLETGVPLRFSGSGSGTDFTFTISSLQPEDIATYYCQQYDHLPLTFGGGTKVAIKRTVAAPSVFIFPPSDEQ (SEQ ID NO:9) 26

CDR1 CDR2 CDR3

Figure 8

ACCATCACTT GTCAGGCGAG TCAGGACATT ACCATTTATT TAAATTGGTA TCAACAGAAA CCAGGGAAAG CCCCT AAGCTCCTGA TCAACGACGC ATCCAGTTTG
GAAACAGGGG TCCCATTAAG GTTCAGTGGA AGTGGATCTG GGACA GATTTTACTT TCACCATCAG CAGCCTGCAG CCTGAAGATA TTGCAACATA TTACTGTCAA
CAGTATGATC ATCTC CCGCTCACTT TCGGCGGCGG GACCAAGGTG GCGATCAAA (SEQ ID NO:10) 9

0919759 3.110599

Figure 9

VSGGSISSGDYYWTWIRQHPGKGLEWIGYIYYSGNTYYNPSLKSRVSMSIDTSENQFSLKLSSVTAADTAVYYCARKPVTGGEDYWGQGTLVTVSS (SEQ ID NO:11) 27

CDR1 CDR2 CDR3

Figure 10

GTCTCTGGTG GCTCCATCAG CAGTGGTGAT TACTACTGGA CCTGGATCCG CCAGCACCCA GGGAAGGGCC TGGAGTGGAT TGGGTACATC TATTACAGTG GGAACACCTA
CTACAACCCG TCCCTCAAGA GTCGAGTTTC CATGTCAATA GACACGTCTG AGAACCAGTT CTCCCTGAAG CTGAGCTCTG TGACTGCCGC GGACACGGCC GTGTATTACT
GTGCGAGAAA ACCAGTGACT GGGGGGGAGG ACTACTGGGG CCAGGGAACC CTGGTCACCG TCTCCTCA (SEQ ID NO:12)

Figure 11

TITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDIVGYYVQQYESLPCGFGQGTKLEIKRTVAAPSVFIFPPSDEQ (SEQ ID NO:13) 28

CDR1 CDR2 CDR3

Figure 12

ACCATCACTT GCCAGGCGAG TCAGGACATT AGTAACTATT TAAATTGGTA TCAGCAGAAA CCAGGGAAAG CCCT AAGCTCCTGA TCTACGATGC TTCCAATTTG GAAACAGGGG
TCCCATCAAG GTTCAGTGGA GTGGATCTG GGACA GATTTTACTT TCACCATCAG CAGCCTGCAG CCTGAAGATG TTGGAACATA TGTCTGTCAA CAGTATGAGA GTCTC
CCGTGCGGTT TTGGCCAGGG GACCAAACTG GAGATCAAA (SEQ ID NO:14)

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Figure 13

VSGGSINSGDFYWSWIRQHPGKGLEWIGYIYYSGSTYYNPSLKSRVTMSIDPSKNQFSLKLISVTAADTAVYYCATSLYYGGGMDVWGQGTTVTVSS (SEQ ID NO:15) 29

CDR1 CDR2 CDR3

Figure 14

GTCTCTGGTG GCTCCATCAA CAGTGGTGAT TTCTACTGGA GCTGGATCCG CCAACACCCA GGGAAGGGCC TGGAGTGGAT TGGGTACATC TATTACAGTG GGAGCACCTA CTACAACCCG TCCCTCAAGA GTCGAGTTAC CATGTCAATA GACCCGTCTA AGAACCAGTT CTCCCTGAAA CTGATCTCTG TGACTGCCGC GGACACGGCC GTTTATTACT GTGCGACNTC CCTTTACTAT GGCGGGGGTA TGGACGTCTG GGGCCAAGGG ACCACGGTCA CCGTCTCCTC A (SEQ ID NO:16)

Figure 15

TITCQASQDISNNLNWYQQKRGNAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISNLQPEDIATYYCQHYDHLPWTFGQGTKVEXKRTVAAPSVFIFPPSDEQ (SEQ ID NO:17) 30

CDR1 CDR2 CDR3

Figure 16

ACCATCACTT GCCAGGCGAG TCAGGACATT AACAACTATT TGAATTGGTA TCAGCAGAGG CCNGGGAACG CCCCT AAACTCCTGA TCTACGATGC ATCCAATTTG GAAACAGGGG TCCCATCAAG GTTCAGTGGA AGTGGATCTG GGACA GATTTTACTT TCACCATCAA CAGCCTGCAG CCTGAAGATA TTGCGACATA TTATTGTCAA CACTATGATC ATCTC CCGTGGACGT TCGGCCAAGG GACCAAGGTG GAANTCAAA (SEQ ID NO:18)

09197593 .110599

Figure 17

VSGGSINNGDYYWSWIRQHPGKGLEWIGHIYYSGSTYYIPSLKSRTTISVDTSKNQFSLKLNSVTAADTAVYYCARGTVTTYYFDYWGQGTTVTVSS (SEQ ID NO:19) 33

CDR1 CDR2 CDR3

Figure 18

GTCTCTGGTG GCTCCATCAA CAATGGTGAT TACTACTGGA GCTGGATCCG CCAGCACCCA GGGAAGGGCC TGGAGTGGAT TGGGCACATC TATTACAGTG GGAGCACCTA
CTACATCCCG TCCCTCAAGA GTCGAACTAC CATATCAGTA GACACGTCTA AGAACCAGTT CTCCCTGAAG CTGAACTCTG TGACTGCCGC GGACACGGCC GTGTATTACT
GTGCGAGAGG GACAGTAACT ACGTACTACT TTGACTACTG GGGCCAGGGA ACCCTGGTCA CCGTCTCCTC A (SEQ ID NO:20) 11

Figure 19

TTTCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGYRTPPECSFGQGTKLEIKRTVAAPSVFIFPPSDEQ (SEQ ID NO: 21) 32

CDR1 CDR2 CDR3

Figure 20

ACCATCACTT GCCGGGCAAG TCAGAGCATT AGCAGCTATT TAAATTGGTA TCAGCAGAAA CCAGGGAAAG CCCCT AAGCTCCTGA TCTATGCTGC ATCCAGTTTG
CAAAGTGGGG TCCCATCAAG GTTCAGTGGC AGTGGATCTG GGACA GATTTCACTC TCACCATCAG CAGTCTGCAA CCTGAAGATT TTGCAACTTA CTACTGTCAA
CAGGGTTACA GAACC CCTCCGGAGT GCAGTTTTGG CCAGGGGACC AAGCTGGAGA TCAAA (SEQ ID NO:22) 12

09197593 .110599

Figure 21

VSGGSVSSGDYYWSWIRQPPGKGLEWIGHLYYSGNTNYNPSLKSRVTISLDTSKNQFSLKLSSVTAADTAVYYCARDFLTGSFFDYWGQGTLVTVSS (SEQ ID NO:24) 33

CDR1 CDR2 CDR3

Figure 22

GTCTCTGGTG GCTCCGTCAG CAGTGGTGAT TACTACTGGA GCTGGATCCG GCAGCCCCCA GGGAAGGGAC TGGAGTGGAT TGGACATCTC TATTACAGTG GGAACACCAA
CTACAACCCC TCCCTCAAGA GTCGAGTCAC CATATCATTA GACACGTCCA AGAACCAGTT CTCCCTGAAG CTGAGCTCTG TGACCGCTGC GGACACGGCC GTGTATTACT
GTGCGAGAGA TTTTTTGACT GGTTCCTTCT TTGACTACTG GGGCCAGGGA ACCCTGGTCA CCGTCTCCTC A (SEQ ID NO:25)

Figure 23

TITCQASQDISNYLNWYQQKPGKAPKLLINDASDLETGVPSRISGSGSGTDFTFTISNLQPEDIATYYCQQYDSLPLTFGGGTKVEIRRTVAAPSVFIFPPSDEQ (SEQ ID NO:26) 34

CDR1 CDR2 CDR3

Figure 24

ACCATCACTT GCCAGGCGAG TCAGGACATA AGCAACTATT TAAATTGGTA TCAGCAGAAA CCAGGGAAAG CCCCT AAGCTCCTGA TCAACGATGC ATCCGATTTG
GAAACAGGGG TCCCATCAAG GATCAGTGGA AGTGGATCTG GGACA GATTTTACTT TCACCATCAG CAACCTGCAG CCTGAAGATA TTGCAACATA TTACTGTCAA
CAATATGATA GTCTC CCGCTCACTT TCGGCGGAGG GACCAAGGTG GAGATCAGA (SEQ ID NO:27)

09187692 .110599

Figure 25

VSGGSVYSGDYYWSWIRQPPGKGLEWIGYIYYSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARDSILGATNYWGQGTLVTVSS (SEQ ID NO:28) 35

CDR1 CDR2 CDR3

Figure 26

GTCTCTGGTG GCTCCGTCTA CAGTGGTGAT TACTACTGGA GCTGGATCCG GCAGCCCCCC GGGAAGGGAC TGGAGTGGAT TGGGTATATC TATTACAGTG GGAGCACCAA TTACAATCCC TCCCTCAAGA GTCGAGTCAC CATATCAGTA GACACGTCCA AGAACCAGTT CTCCCTGAAG CTGAGCTCTG TGACCGCTGC GGACACGGCC GTGTATTACT GTGCGAGAGA CTCCATACTG GGAGCTACCA ACTACTGGGG CCAGGGAACC CTGGTCACCG TCTCCTCA (SEQ ID NO:29) 15

Figure 27

TITCQASQXISNYLXWYQQKPGKAPKXLISDASNLETGVPSRFSGSGSGTXXTFTISSLQPEDIATYHCXQYXSLPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQ (SEQ ID NO:30) 30

CDR1 CDR2 CDR3

Figure 28

ACCATCACTT GCCAGGCGAG TCNGGACATT AATAACTATT TANATTGGTN TCAGCAGAAA CCAGGGAAAG CCCCT AAASTCCTGA TCTCCGATGC ATCCAATTTA GAAACAGGGG TCCCATCGAG GTTCAGTGGA AGTGGATCTG GGACA GANTNTACTT TCACCATCAG CAGCCTGCAG CCTGAAGATA TTGCNACATA TCACTGTCNA CAGTATNATA GTCTC CCGCTCACTT TCGGCGGAGG GACCAAGGTA GAGATCAAA (SEQ ID NO:31) 18

09197693 .110599

Figure 29

VSGGSVSSGDYYWTWIRQSPGKGLEWIGHIYYSGNTNYNPSLKSRLTISIDTSKTQFSLKLSSVTAADTAIYYCVRDRVTGAFDIWGQGTMVTSS (SEQ ID NO:32) 37

CDR1 CDR2 CDR3

Figure 30

GTCTCTGGTG GCTCCGTCAG CAGTGGTGAT TACTACTGGA CCTGGATCCG GCAGTCCCCA GGGAAGGGAC TGGAGTGGAT TGGACACATC TATTACAGTG GGAACACCAA TTATAACCCC TCCCTCAAGA GTCGACTCAC CATATCAATT GACACGTCCA AGACTCAGTT CTCCCTGAAG CTGAGTTCTG TGACCGCTGC GGACACGGCC ATTTATTACT GTGTGCGAGA TCGAGTGACT GGTGCTTTTG ATATCTGGGG CCAAGGGACA ATGGTCACCG TCTCTTCA (SEQ ID NO:33) 17

Figure 31

TITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDIATYFCQHFDHLPLAFGGGTKVEIKRTVAAPSVFIFPPSDEQ (SEQ ID NO:34) 38

CDR1 CDR2 CDR3

Figure 32

ACCATCACTT GCCAGGCGAG TCAGGACATC AGCAACTATT TAAATTGGTA TCAGCAGAAA CCAGGGAAAG CCCCT AAACTCCTGA TCTACGATGC ATCCAATTTG GAAACAGGGG TCCCATCAAG GTTCAGTGGA AGTGGATCTG GGACA GATTTTACTT TCACCATCAG CAGCCTGCAG CCTGAAGATA TTGCAACATA TTTCTGTCAA CACTTTGATC ATCTC CCGCTCGCTT TCGGCGGAGG GACCAAGGTG GAGATCAAA (SEQ ID NO:35) 18

09197593 .110599

Figure 33

Amino Acid Sequences and Structure of Human Heavy Chain Derived from EGFR-Specific Hybridomas

```
Human γ2         CDR1                    CDR2                                                          CDR3
4-31    VSGGSIS SGGYYWS WIRQHPGKGLEWIG YIYYSGSTYYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCAR                              ASTKGPSVFPPLAPCSRSTST
E1.1    ------N--D------------------DC-----------------------------------F---T-------------- STVVNPG  WFDP  WGQGYLVTVSS  ---------------------
E2.4    ------N--D---------------------S-----N-F-----------L----------------------C---- NIVTTG   AFDI  WGQGTMVTVSS  ---------------------
E2.5    --------D---T------------------------N-----------SM-I---E------------------------ KPVTGG   EDY   WGQGTLVTVSS  ---------------------
E6.2    ------N--DF--------------------------------------M-I-P---------I---------------T SLYYGG   GMDV  WGQGTTVTVSS  ---------------------
E6.4    ------NN-D----------------------H---------I-------T--------------N---------------- GTVTTYY  YFDY  WGQGTTVTVSS  ---------------------

                 CDR1                    CDR2                                                          CDR3
4-61    VSGGSVS SGSYYWS WIRQPPGKGLEWIG YIYYSGSTNYNPSLKS RVTISVDTSKNQFSLKLSSVTAADTAVYYCAR
E2.11   ---------D-----------------------HL----N--------------L----------------------------- DFLTGSF  FDY   WGQGTMVTVSS  ---------------------
E6.3    ------Y--D-------------------------------------------------------------------------- DSILGA   TNY   WGQGTLVTVSS  ---------------------
E7.6.3  ---------D---T----S----------H-----N-----------L---I----T---------------I---V- DRVTGA   FDI   WGQGTMVTVSS  ---------------------
```

Figure 34

Amino Acid Sequence and Structure of Human Kappa Chain Derived from EGFR-Specific Hybridomas

```
                         Vκ SEGMENT                                              Jκ SEGMENT
              CDR1                    CDR2                          CDR3
Vκ (O12)
Human Cκ     TITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDIATYYCQQYDNLP                RTVAAPSVFIFPPSDEQ
EGF.1.1.K    ----------N-----F---------V--H--------G-----------------G-------------ES--   LTFGGGTKVEIK  ----------------
EGF.2.4.K    ----------TI------------------N---S-----L-----------------------------H--    LTFGGGTKVAIK  ----------------
EGF.2.5.K    ------------------------------------------------------------VG--V---ES--     CGFGQGTKLEIK  ----------------
EGF.2.11.K   ------------------------------N---D------I-------------N--------------S--    LTFGGGTKVEIR  ----------------
E6.2.K       -----------N-------R-N-------------------------------N-----------H--H--      WTFGQGTKVEXK  ----------------
E6.3.K       -------X--N--X-----------X--S-----------------XX-------------H-X--XS--       LTFGGGTKVEIK  ----------------
E6.4.K*      ---R---S--S-------------------A--S-QS---------------L---------F-------GYRT-PE  CSFGQGTKLEIK  ----------------
*O12 gene
E7.6.3.K     --------------------------------------------------------------------F--HF-H--   LAFGGGTKVEIK  ----------------
```

Figure 35

ABX-EGF: Blockage of EGF Binding to Human Epidermoid Carcinoma A431 Cells

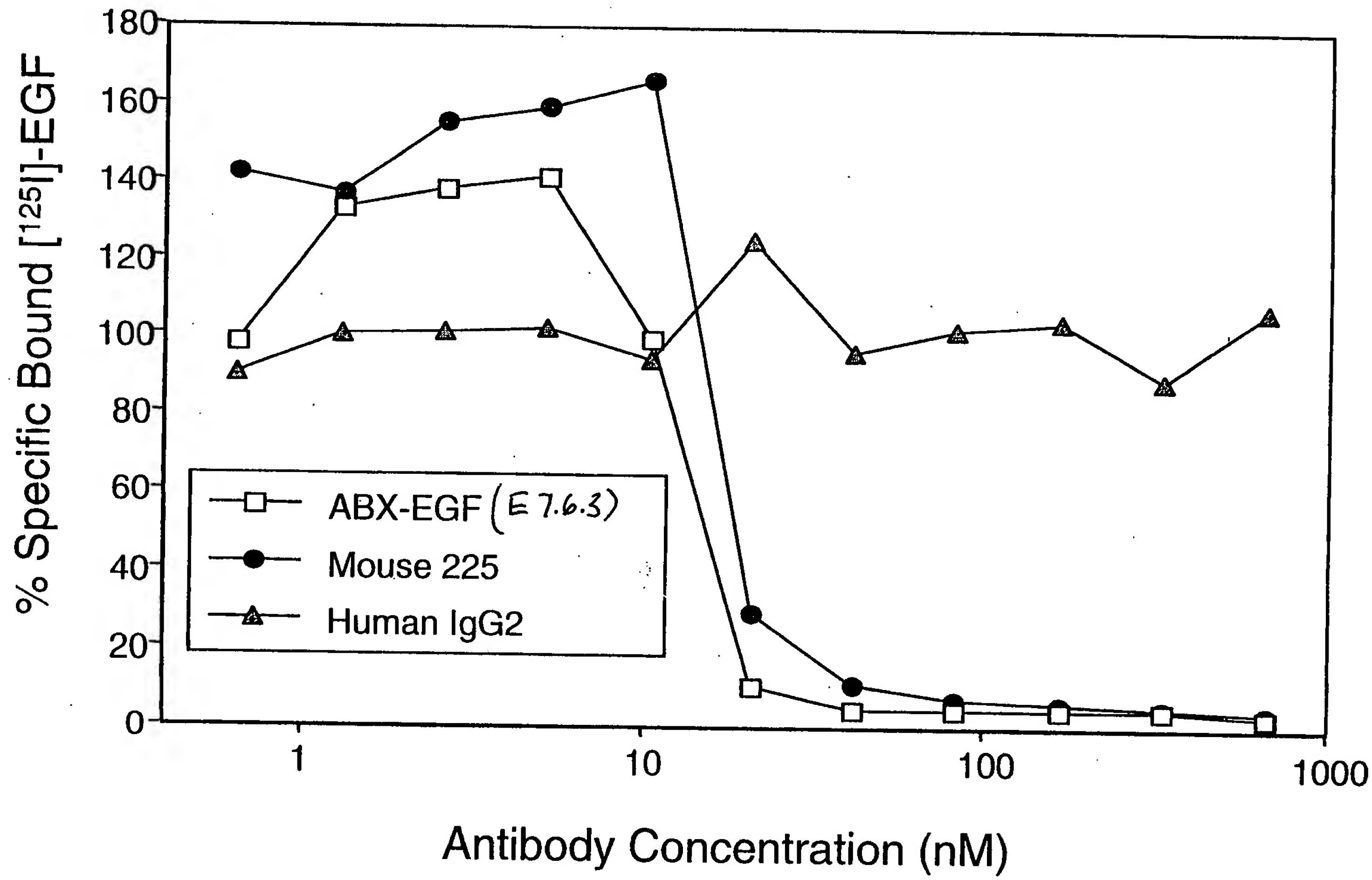
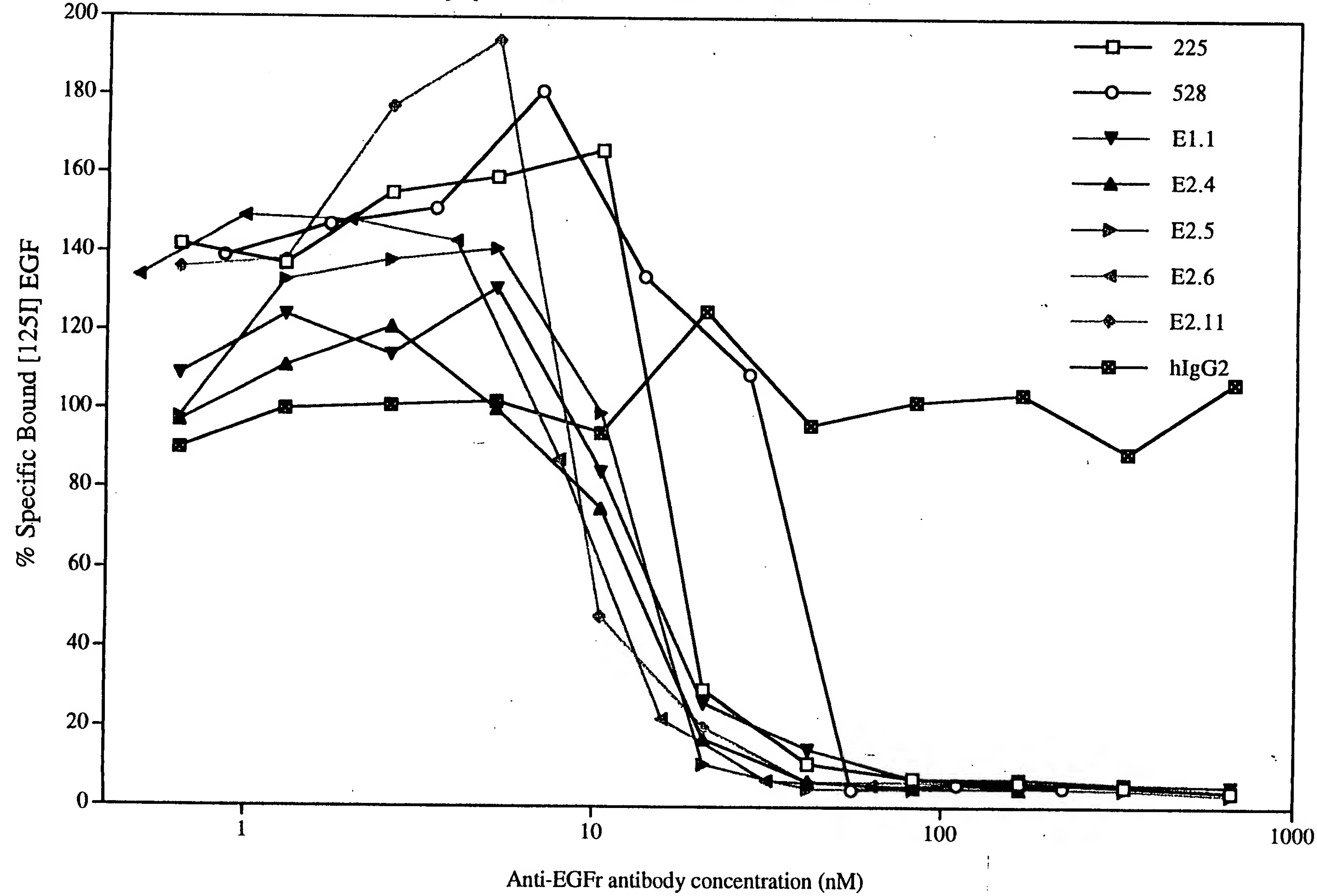


Figure 36

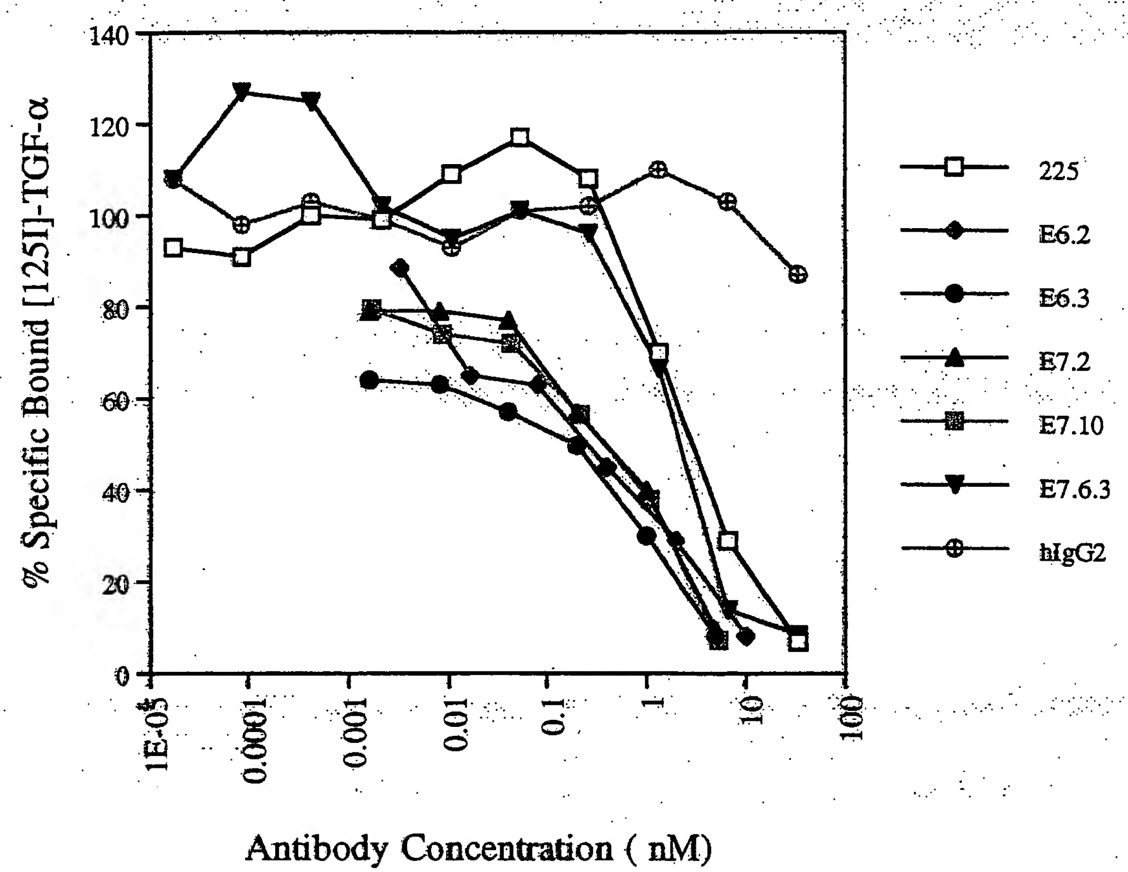
Inhibition of EGF binding to EGF receptors on A431 cells by purified anti-EGFr antibodies



Background=0.1nM [125I]EGF=1016 cpm

-26-96-g2-EGF/A431

Inhibition of TGF-α binding to A431 cells
by anti-EGF receptor antibodies



09507143.031601

Figure 37

Figure 38

ABX-EGF: Blockage of EGF Binding to Human Colon Adenocarcinoma SW948 Cells

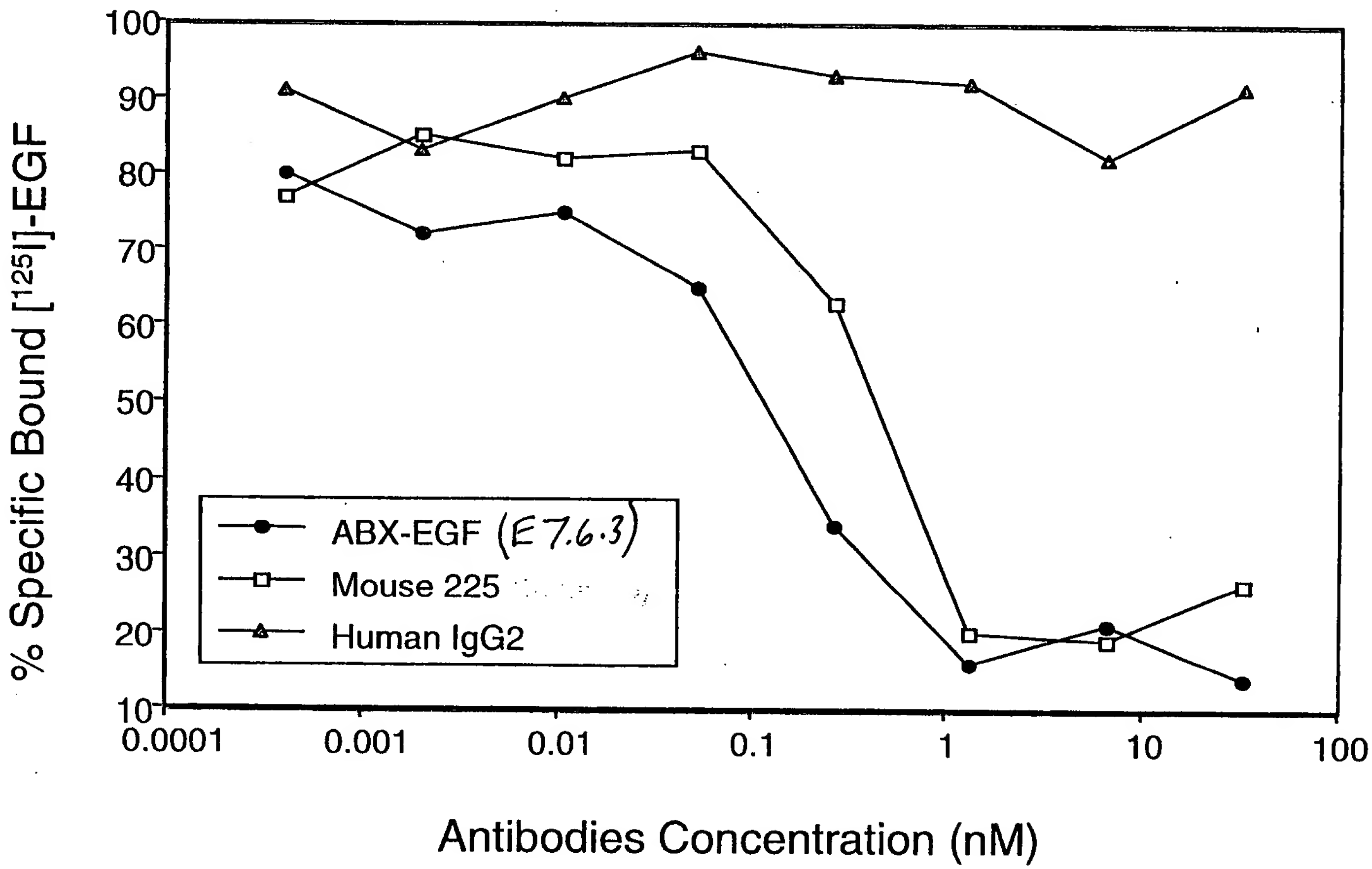


Figure 39

ABX-EGF: Inhibition of Human Colon Adenocarcinoma (SW948) Growth *In Vitro*

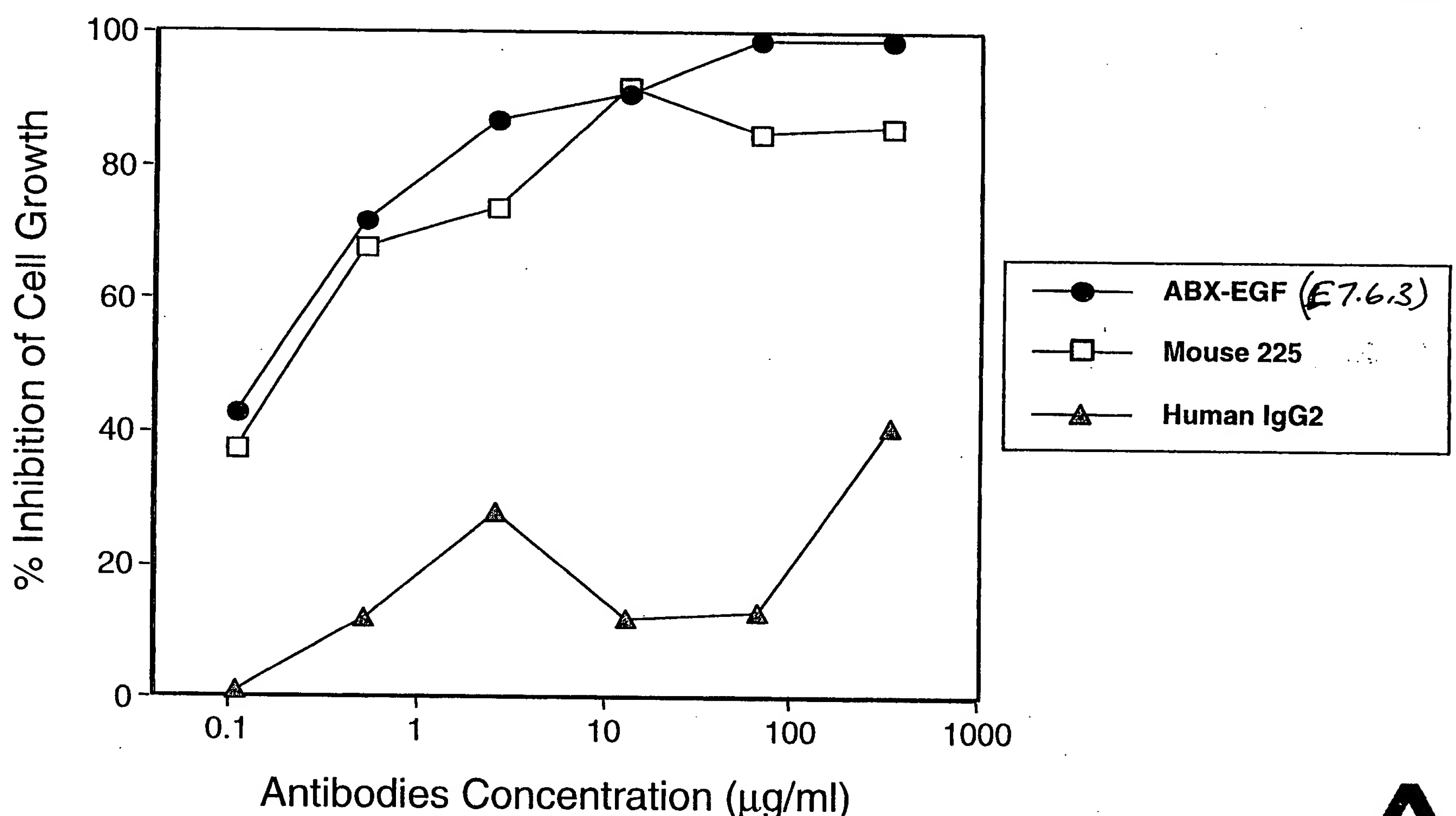
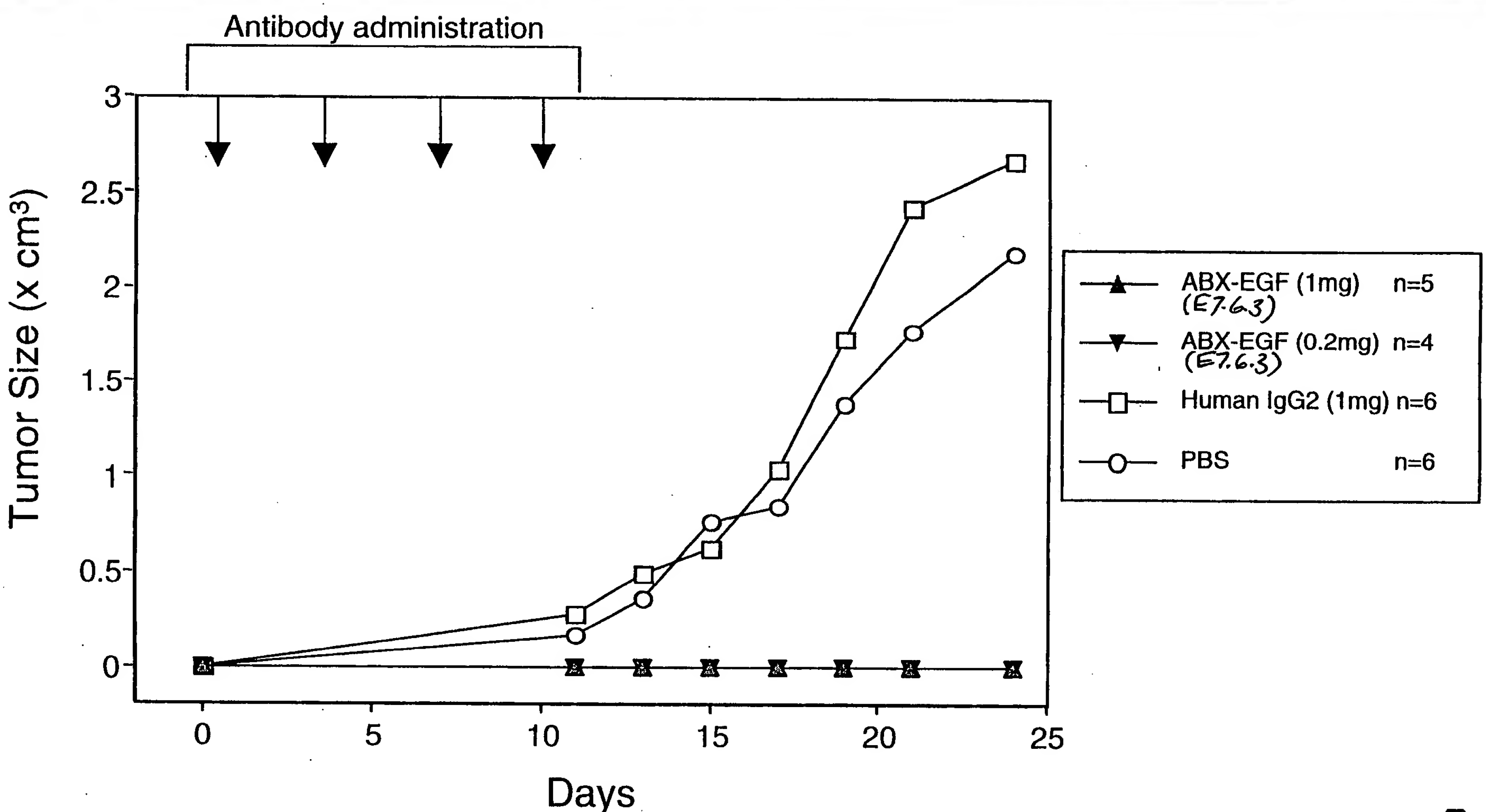


Figure 40

ABX-EGF: Inhibition of Human Epidermoid Carcinoma Growth in Nude Mice



5 x 10^6 A431 cells injected at day 0

Figure 41

Inhibition of Human Epidermoid Carcinoma Formation in Nude Mice by ABX-EGF

Treatment	Dose (mg)	Tumor Formation[b] (incidence)	Tumor size[c] (cm^3)
PBS		6/6	1.376
Human IgG2[a]	1	6/6	1.727
E7.6.3	1	0/5	0
	0.2	0/4	0
E2.5	1	0/3	0
	0.2	0/3	0
E1.1	1	0/3	0

[a] control human myeloma IgG2

[b] incidence determined 19 days post tumor inoculation

[c] tumor size measured 19 days post tumor inoculation

Figure 42

ABX-EGF: Prevention of Human Tumor Formation in Nude Mice

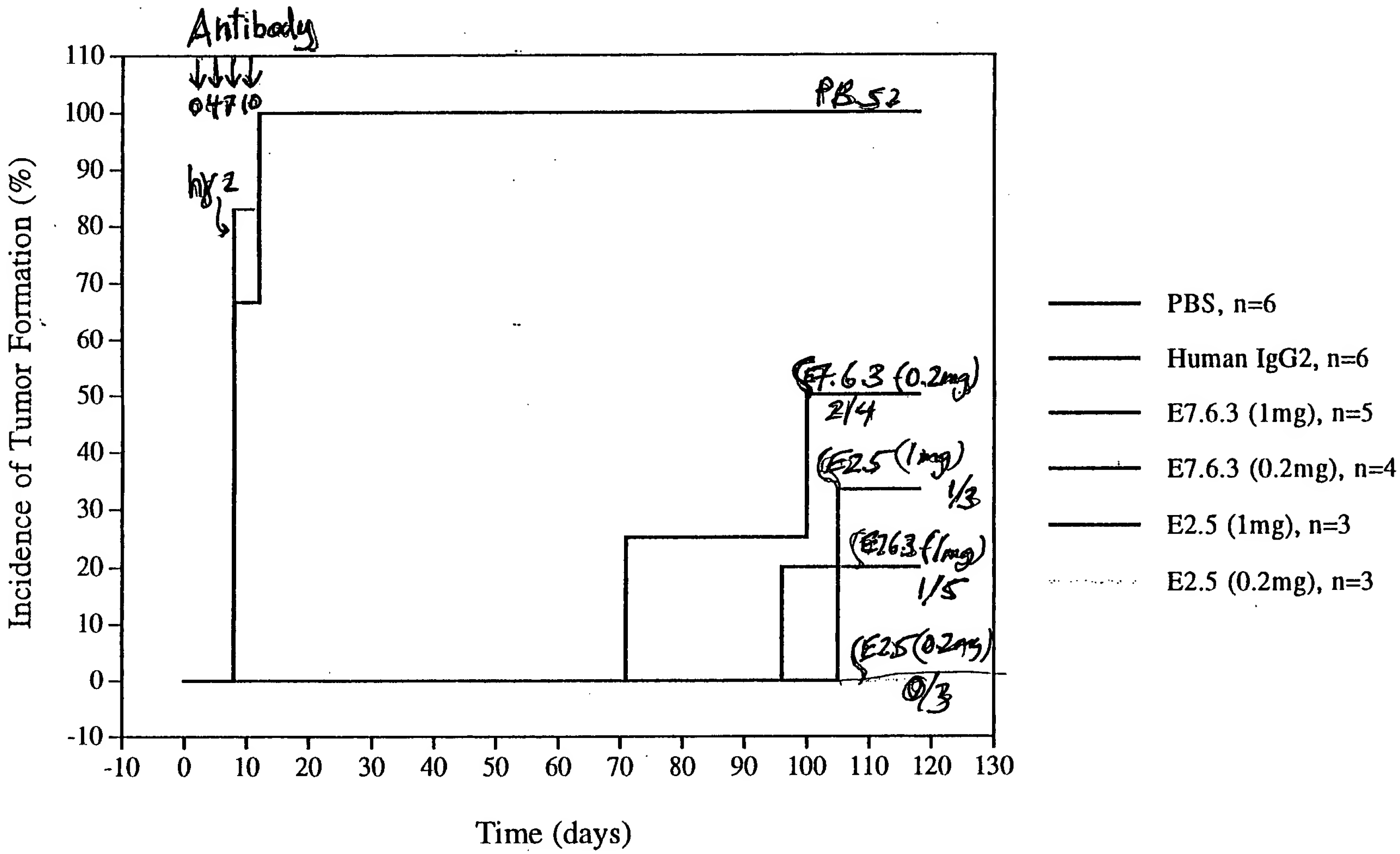
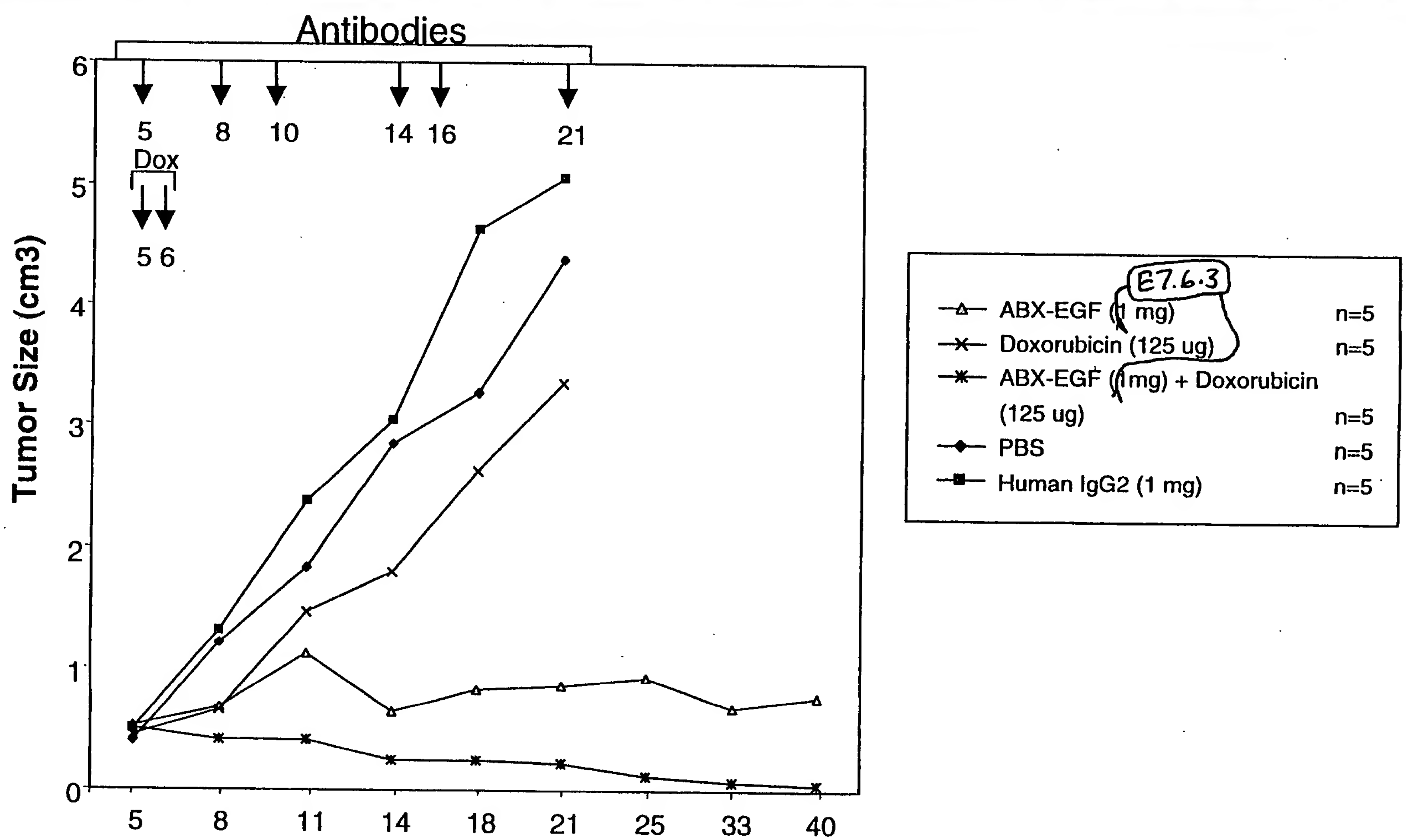


Figure 43

Eradication of Established Human Epidermoid Tumor in Nude Mice by ABX-EGF (E7.6.3)



A431 (5 x 10^6/mouse) were injected at day 0

Figure 44

Eradication of Established Human Epidermoid Tumor in Nude Mice by ABX-EGF (E2.5)

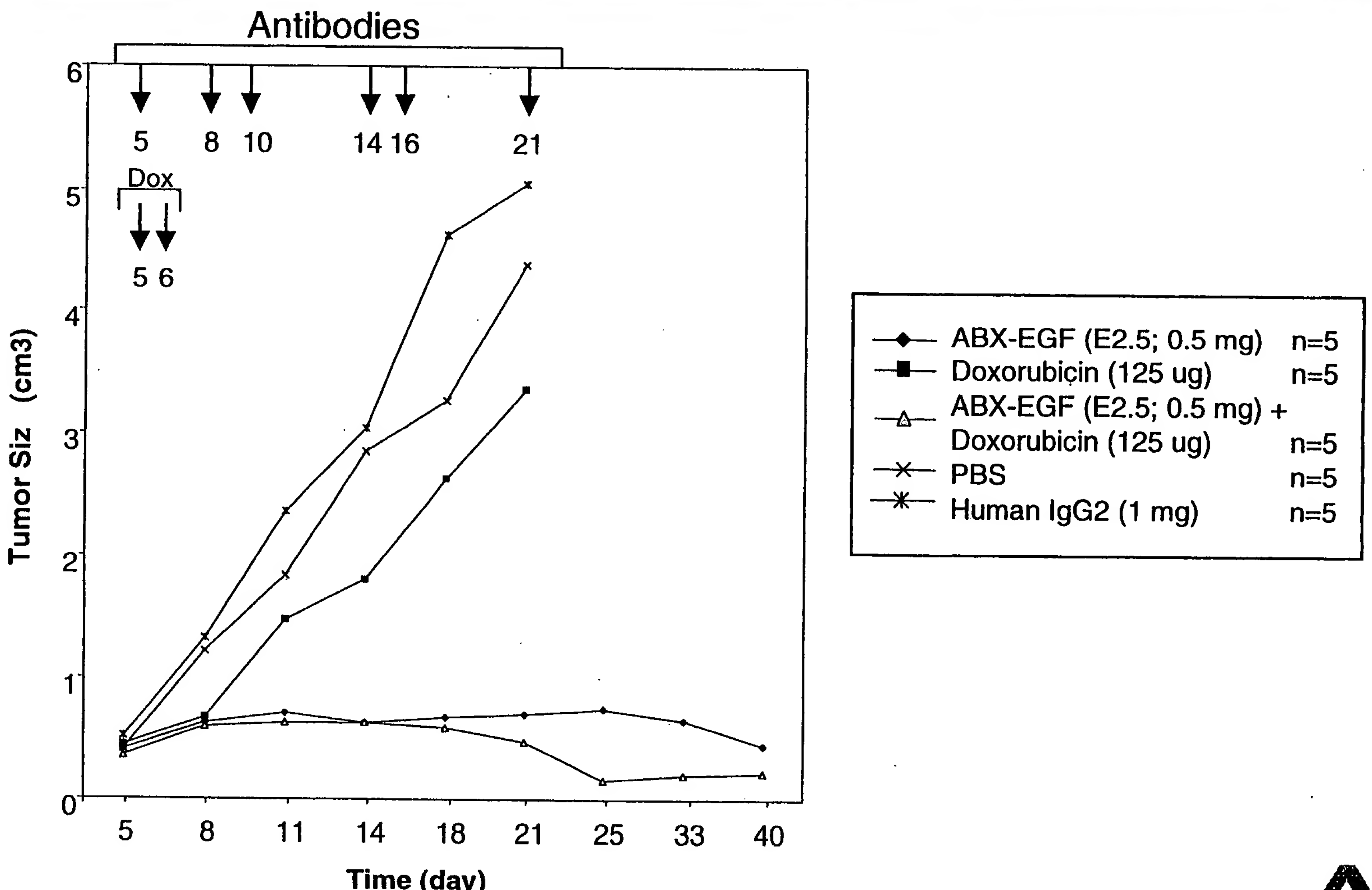
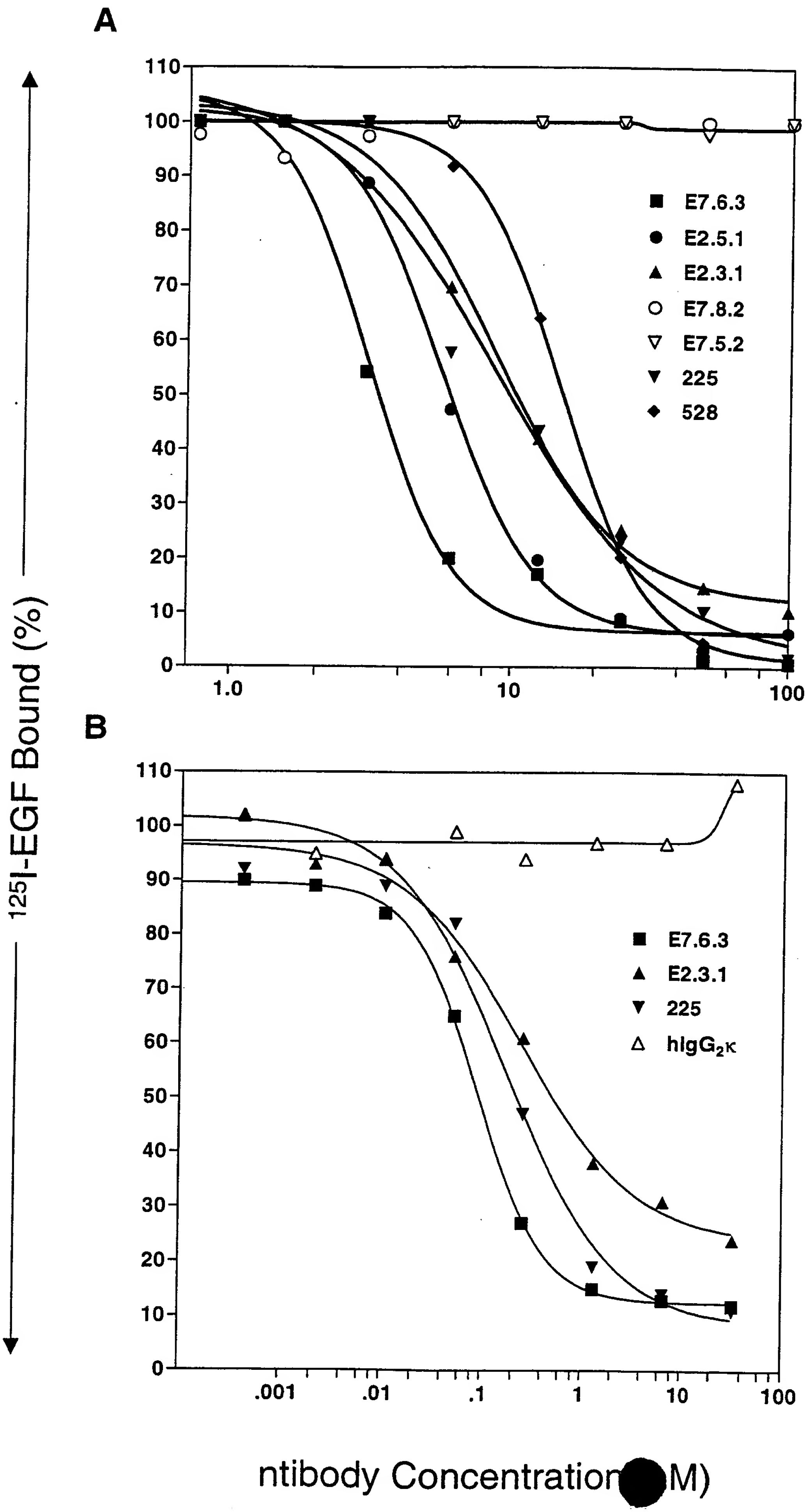


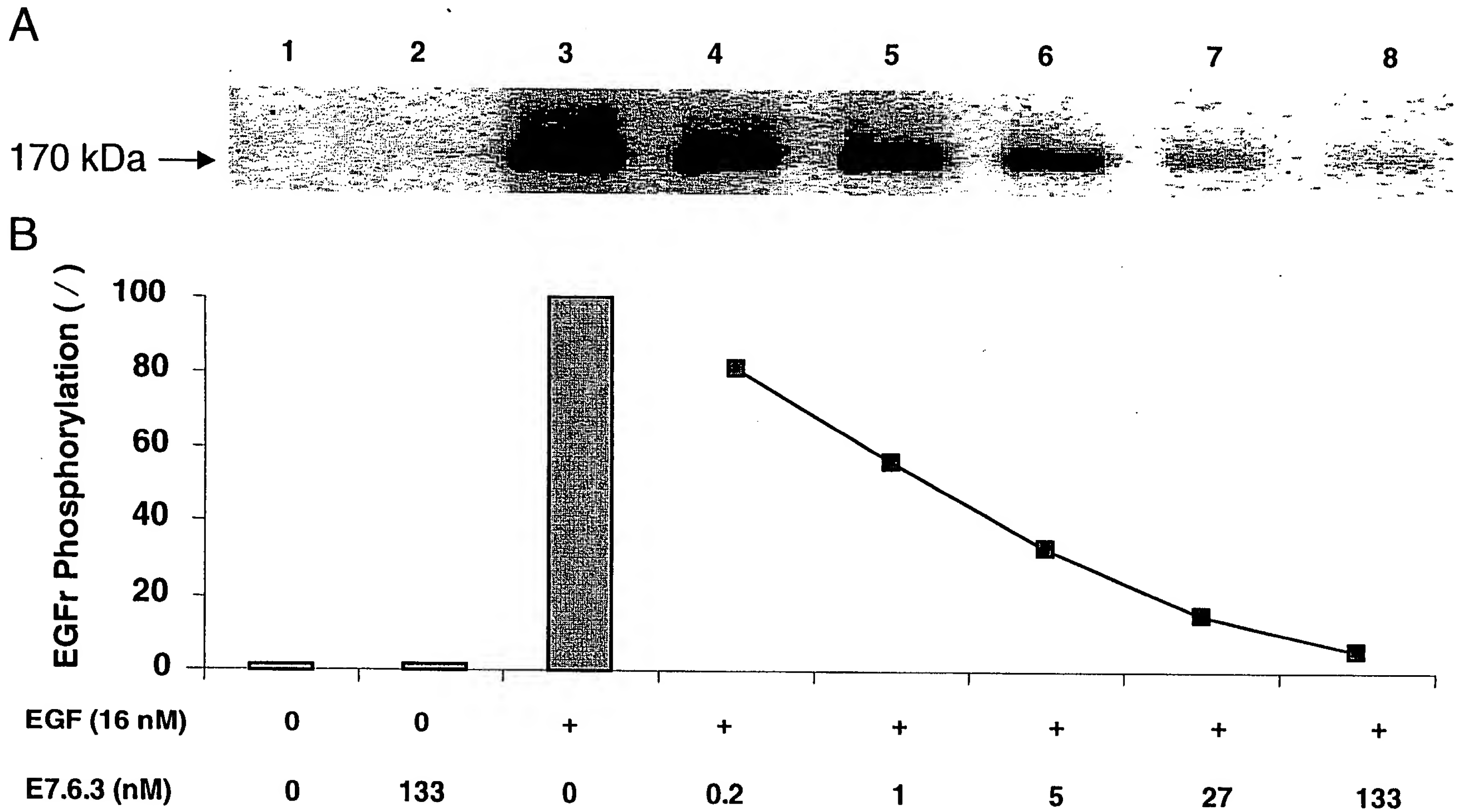
Fig. 45


A
110
100
90
80
70
60
50
40
30
20
10
0
1.0
10
100
E7.6.3
E2.5.1
E2.3.1
E7.8.2
E7.5.2
225
528
B
110
100
90
80
70
60
50
40
30
20
10
0
.001
.01
.1
1
10
100
E7.6.3
E2.3.1
225
hIgG2κ
125I-EGF Bound (%)
ntibody Concentration M)

1=45

Fig. 46

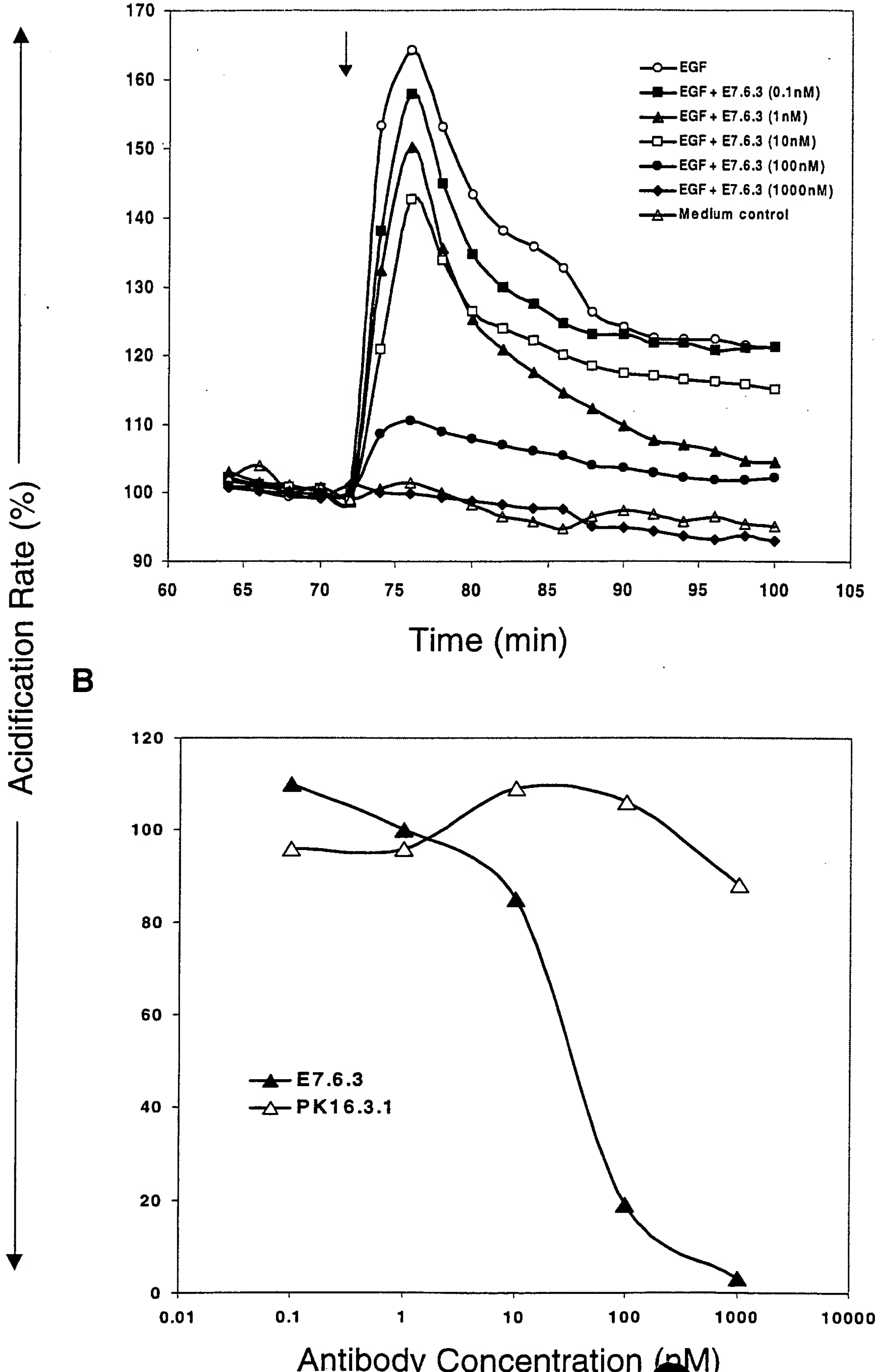
22/46



A
1
2
3
4
5
6
7
8
170 kDa
B
EGFr Phosphorylation (/)
100
80
60
40
20
0
EGF (16 nM) 0 0 + + + + + +
E7.6.3 (nM) 0 133 0 0.2 1 5 27 133

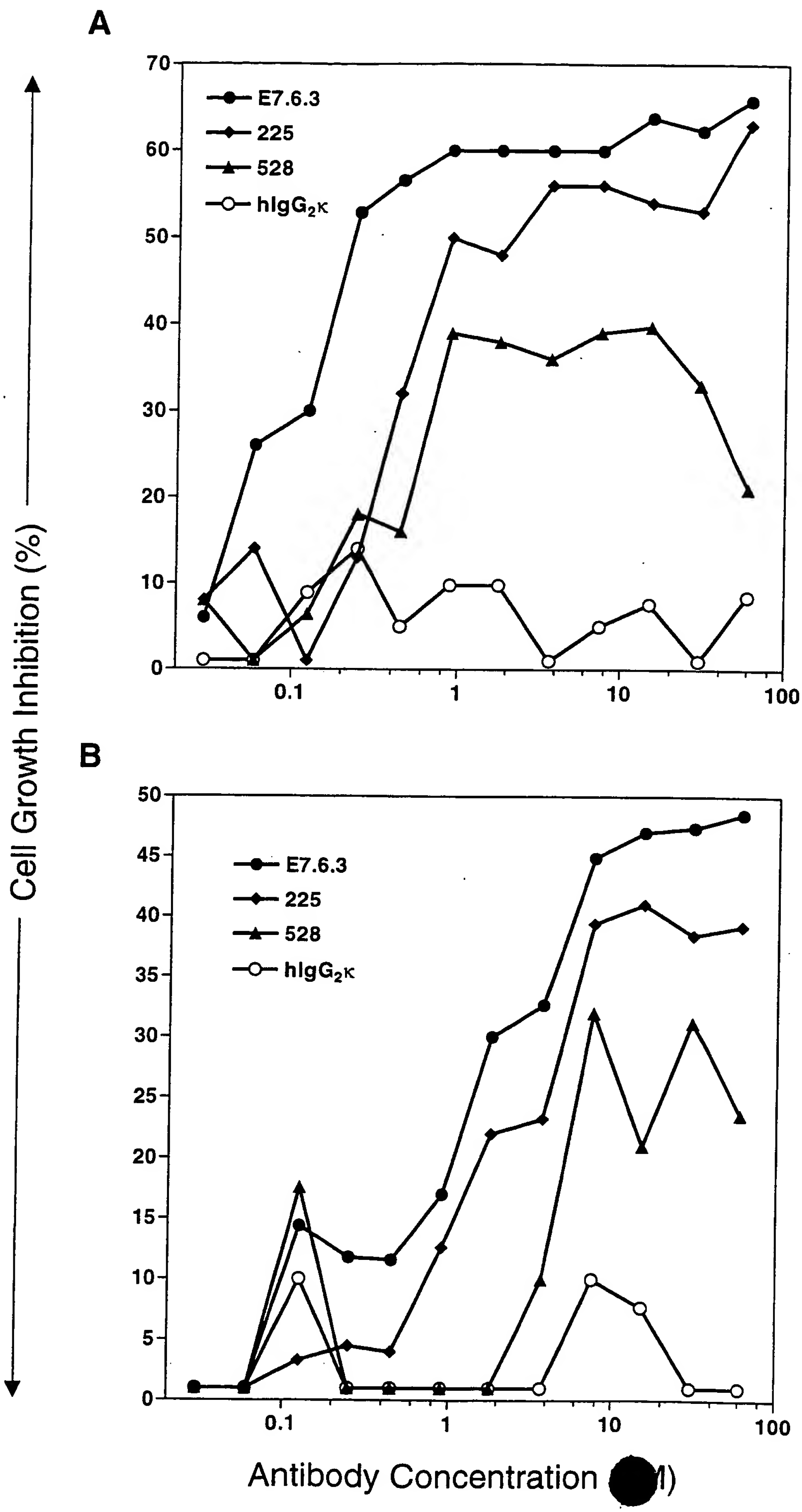
Fig. 47

A


Acidification Rate (%)
EGF
EGF + E7.6.3 (0.1nM)
EGF + E7.6.3 (1nM)
EGF + E7.6.3 (10nM)
EGF + E7.6.3 (100nM)
EGF + E7.6.3 (1000nM)
Medium control
170
160
150
140
130
120
110
100
90
60
65
70
75
80
85
90
95
100
105
Time (min)
B
120
100
80
60
40
20
0
0.01
0.1
1
10
100
1000
10000
E7.6.3
PK16.3.1
Antibody Concentration (nM)

3=47

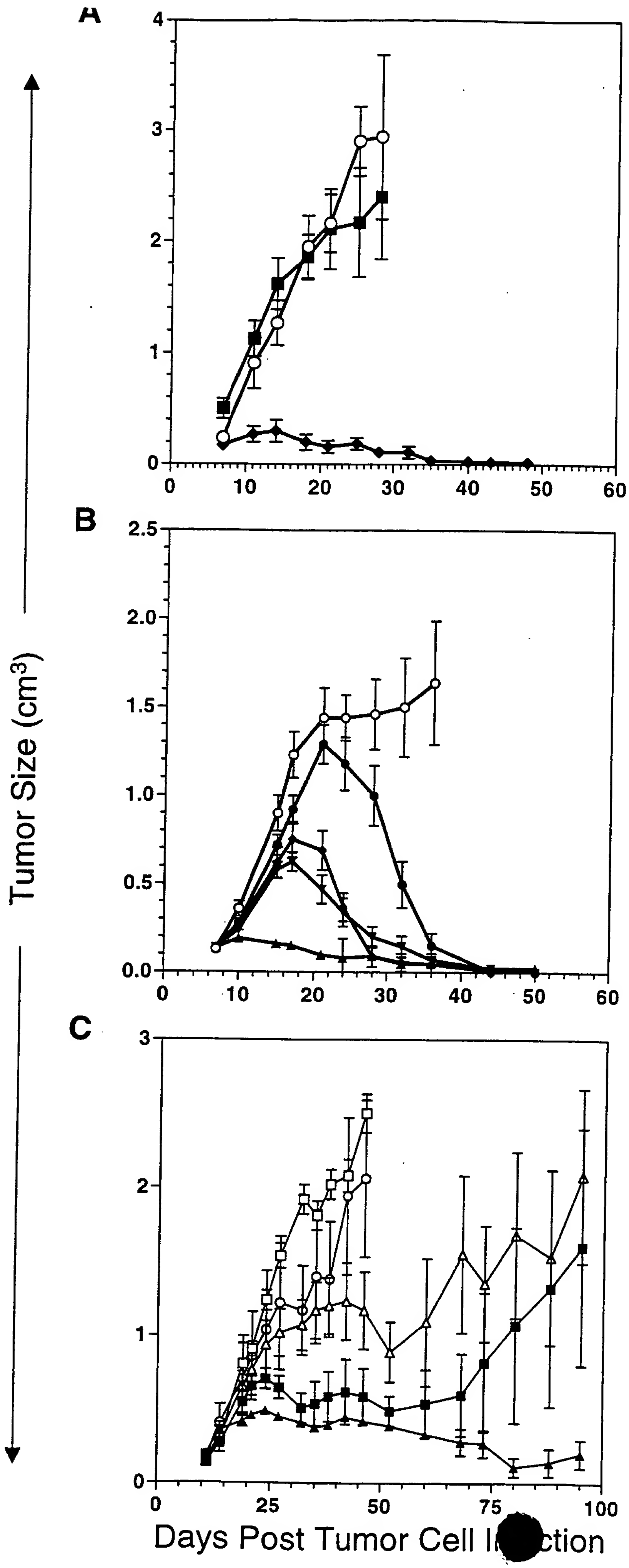
Fig. 48



09167592.041598

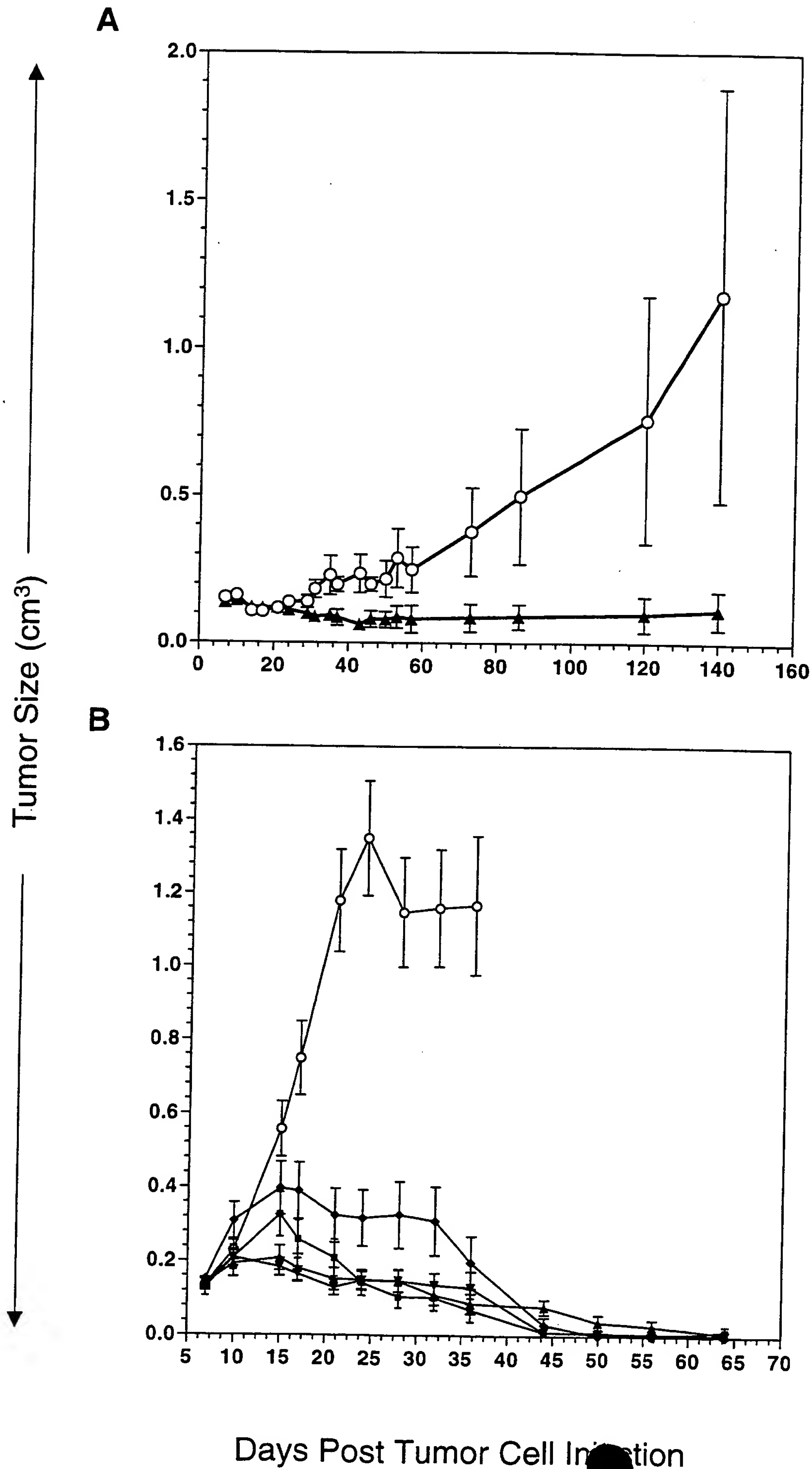
4-48

Fig. 49


A
B
C
Tumor Size (cm^3)
4
3
2
1
0
0
10
20
30
40
50
60
2.5
2.0
1.5
1.0
0.5
0.0
0
10
20
30
40
50
60
3
2
1
0
0
25
50
75
100
Days Post Tumor Cell I ction

5E49

Fig. 50



09197592.110502

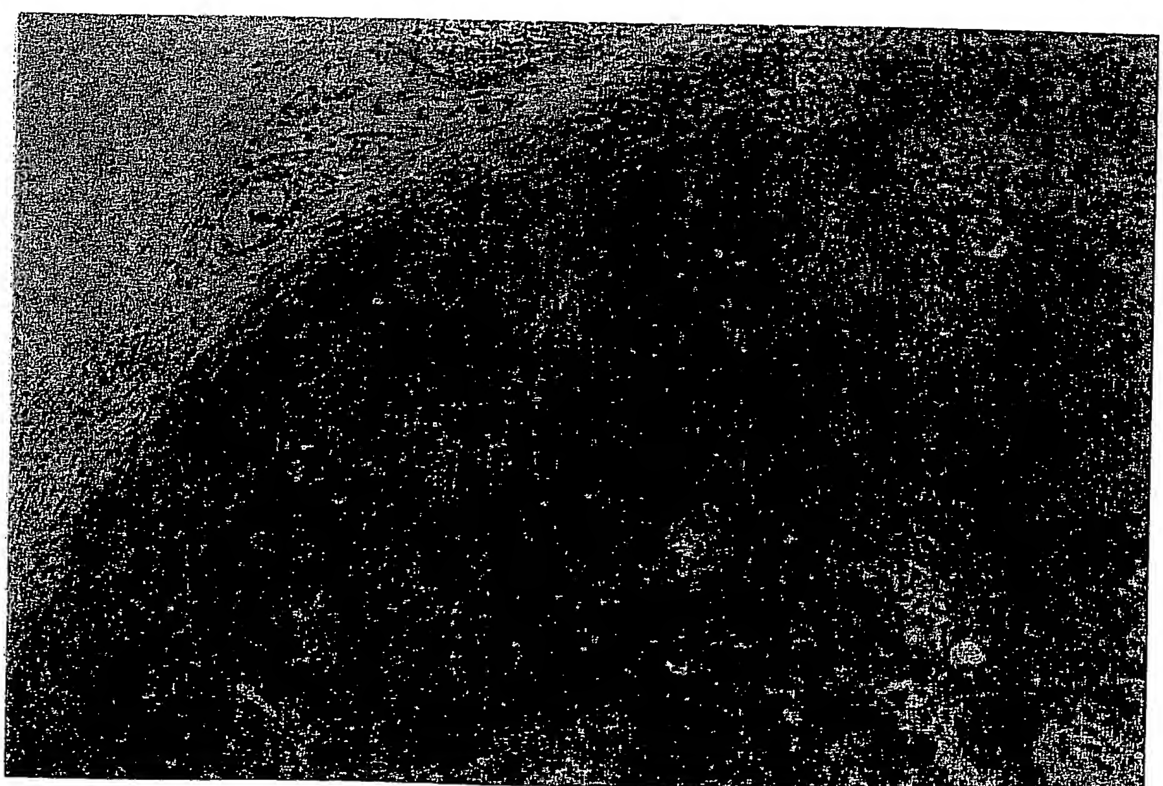
6=50

Fig. 51

Figure 7

A.

B.



7=51

Fig. 52

Time	Incidence of Tumor Formation			
(day)	PBS	PK16.3.1 (1 mg)	E7.6.3 (0.2 mg)	E7.6.3 (1 mg)
0	0/5	0/5	0/10	0/10
3	4/5	0/5	0/10	0/10
8	4/5	3/5	0/10	0/10
10	5/5	5/5	0/10	0/10
25	5/5	5/5	0/10	0/10
100	ND	ND	0/10	0/10
250	ND	ND	0/10	0/10

09197692 .110599

Table 1=52

Fig. 53

Treatment (dose/injection)	Total Dose	Total No. of Mice	Tumor-free Mice on Day 60	
			No.	%
None		71	0	0
Control $IgG_2\kappa$ (1 mg)	6 mg	16	0	0
E7.6.3 (1 mg)	6 mg	50	50	100
E7.6.3 (0.5 mg)	3 mg	20	19	95
E7.6.3 (0.25 mg)	1.5 mg	5	3	60
E7.6.3 (0.2 mg)	1.2 mg	19	5	26
E7.6.3 (0.1 mg)	0.6 mg	20	13	65
E7.6.3 (0.05 mg)	0.3 mg	15	1	7

09187693.110599

Table2=53

Fig. 54

Inhibitory Effects of E7.6.3 on EGF-induced Tyrosine-phosphorylation and Degradation of EGFr in Cultured A431 Cells

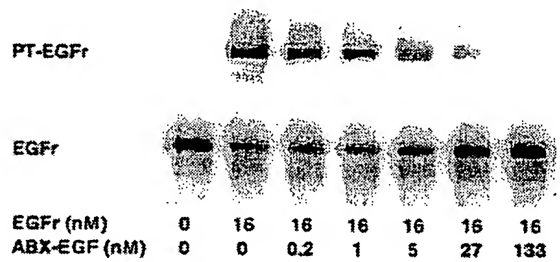


Fig. 55

Preliminary Results Obtained Comparing

Inhibitory Effects of ~~ABX-EGF~~ E7.6.3 and 225 on EGF-induced Tyrosine-phosphorylation and Degradation of EGFr in Cultured A431 Cells

Fig. 56

Preliminary Results Obtained Comparing

Effects of EGF, ABX-EGF and 225 on Tyrosine-phosphorylation and Degradation of EGFr in Cultured A431 Cells

EGF (nM)	0	0	0	1.6	1.6	1.6	16	16	16	160	160	160
ABX-EGF (133nM)	-	+	-	-	+	-	-	+	-	-	+	-
225 (133nM)	-	-	+	-	-	+	-	-	+	-	-	+

CGTF 20.1 Heavy

V – DP50 / hv30
DXp4

E20.1MG30.Seq Sequence

Fig. 57

```
          10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
GCGATCCAGC CTTTTAGGTC CATGCCNTTC TCCTGTGNAG CGTCTGGATT    50
A  I  Q  P   F  R  S   M  P  F   S  C  X  A   S  G  F

CCCCTTCAGT AGNTNTGGCA TGCACTGGGT CCGCCAGGCT CCAGGCAAGG   100
 P  F  S   X  X  G  M   H  W  V   R  Q  A   P  G  K  G

GGCTGGAGTG GGTGGCAGTT ATATGGTATG ATGGAAGTAA TAAATACTAT   150
 L  E  W   V  A  V   I  W  Y  D   G  S  N   K  Y  Y

GCAGACTCCG TGAAGGGCCG ATTCACCATC TCCAGAGACA ATTCCAAGAA   200
A  D  S  V   K  G  R   F  T  I   S  R  D  N   S  K  N

CACGCTGTAT CTGCAAATGA ACAGACTGAG AGCCGAGGAC ACGGCTGTGT   250
 T  L  Y   L  Q  M  N   R  L  R   A  E  D   T  A  V  Y

ATTACTGTGC GAGATTTTTG GAGTGGTTAC CCTTTGACTA CTGGGGCCAG   300
 Y  C  A   R  F  L   E  W  L  P   F  D  Y   W  G  Q

GGAACCCTGG TCACCGTCTN CTCAGACTCC ACCAAGGGCC CATCGGTCTT   350
G  T  L  V   T  V  X   S  D  S   T  K  G  P   S  V  F

CNCCCTGGCG CCCTGCTTCC AGGAGCACCC TCNGANAGCA CANANGGCCC   400
 X  L  A   P  C  F  Q   E  H  P   X  X  A   X  X  A  P

CTGGGACTGN CTGNTACAAG GACTNCTTTC CCTCNAACCN GGTGACCNTN   450
 G  T  X   X  Y  K   D  X  F  P   S  N  X   V  T  X

TCNTGGGAAA CTCAGNGCNC NTCTNNATNA C                       481
S  W  E  T   Q  X  X   S  X  X
```

2/23/98

Jk- Jk3

Fig. 58

E20.1VK.Seq Sequence

```
         10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
GGAACCTTTN GGTTCGCNCC TTTTGGAGNC AGACCCANCA TCACTTGTCG     50
 G  T  F  X   F  A  P   F  G  X   R  P  X  I   T  C  R

GGCGAGTCAG GGCATTAGCA ATTTTTTAGC CTGGTTTCAG CAGAAACCAG    100
  A  S  Q   G  I  S  N   F  L  A   W  F  Q   Q  K  P  G

GGATAGCCCC TAAGTCCCTG ATCTATGCTG CATCCACTTT GCAAAGTGGG    150
   I  A  P   K  S  L   I  Y  A  A   S  T  L   Q  S  G

GTCCCATCAA AGTTCACCGG CAGTGGATAT GGGACAGATT TCACTCTCAC    200
 V  P  S  K   F  T  G   S  G  Y   G  T  D  F   T  L  T

CATCAGCAGC CTGCAGCCTG AAGACTTTGC AACTTATTAT TGTCAACAAT    250
  I  S  S   L  Q  P  E   D  F  A   T  Y  Y   C  Q  Q  Y

ATAATGTTTA CCCATTCACT TTCGGCCCTG GGACCAAAGT GGATATCAAA    300
   N  V  Y   P  F  T   F  G  P  G   T  K  V   D  I  K

CGAACTGTGG CTGCACCATC TGTCTTCATC TTCCCGCCAT CTGATGAGCC    350
 R  T  V  A   A  P  S   V  F  I   F  P  P  S   D  E  P

AGTTGAAATC TGGAACTGCC TCTGTTGTGT GCCTGCTGAA TAACTTCTAT    400
  V  E  I   W  N  C  L   C  C  V   P  A  E   .  L  L  S

CCCAGAGAGG CCAAAGTACA GTGGAAGGTG GATAACGCCN CNNTTGGCGG    450
  Q  R  G   Q  S  T   V  E  G  G   .  R  X   X  W  R

NNTCCTTTCN CTCNCCCNTC CTCNNCCCNC CTCTCNCNA                489
X  P  F  X   X  P  S   S  X  X   L  S  X
```

2/23/98

D- JH- JH4b Fig. 59


```
          10          20          30          40          50
 1234567890  1234567890  1234567890  1234567890  1234567890
 AAGCCTGTTG  CCTCAGTGCA  GGTCTCCTGC  AAGGCTTCTG  GATACACCTT    50
 K  P  V  A    S  V  Q    V  S  C    K  A  S  G    Y  T  F

 CACCAGTTAT  GATATCAACT  GGGTGCGACA  GGCCACTGGA  CAAGGGCTTG   100
  T  S  Y    D  I  N  W    V  R  Q    A  T  G    Q  G  L  E

 AGTGGATGGG  ATGGATGAAC  CCTAACAGTG  GTAACACAGG  CTATGCACAG   150
  W  M  G    W  M  N    P  N  S  G    N  T  G    Y  A  Q

 AAGTTCCAGG  GCAGAGTCAC  CATGACCAGG  AACACCTCCA  TAAGCACAGC   200
 K  F  Q  G    R  V  T    M  T  R    N  T  S  I    S  T  A

 CTACATGGAG  CTGAGCAGCC  TGAGATCTGA  GGACACGGCC  GTGTATTACT   250
  Y  M  E    L  S  S  L    R  S  E    D  T  A    V  Y  Y  C

                   DIR           DN1       DK1
 GTGCGAGAGG  AGGCCCCTAT  AGCAGTGGCT  GGACCTTCTT  TGACTACTGG   300
  A  R  G    G  P  Y    S  S  G  W    T  F  F    D  Y  W

 GGCCAGGGAA  CCCTGGTCAC  CGTCTCCTCA  GCCCTNCACC  AAGGGCCCAT   350
 G  Q  G  T    L  V  T    V  S  S    A  L  H  Q    G  P  I

 CGGTCTTCCC  CCTGGCGCCC  TGCTCCAGGA  GCACCTCCCA  GAGCACANTC   400
  G  L  P    P  G  A  L    L  Q  E    H  L  P    E  H  X  X

 NNCCCTTGGG  CTGCCTGGNN  CAAGGACTCT  TTCCCCNAAC  CCCGGNTGA    449
  P  L  G    C  L  X    Q  G  L  F    P  X  T    P  X
```

DN1 [illegible]

2/23/98

CDR E20.3 Kappa

V-B3/DPK24
JK-JK4

Fig. 60

E20.3VK.Seq Sequence

```
         10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
TTTGAACCCT TCNTGGCCGT GTCTCTNGGC GCGAGGGCCA CCATCAACTG    50
F  E  P  F   X  A  V   S  L  G   A  R  A  T   I  N  C

CAAGTCCAGC CAGCGTGTTT TATACANCTC CAACAATAAG AACTGCTTAG   100
 K  S  S   Q  R  V  L   Y  X  S   N  N  K   N  C  L  A

CTTGGTACCA GCAGAAACCA GGACAGCCTC CTAAGCTGCT CATTTACTGG   150
  W  Y  Q   Q  K  P   G  Q  P  P   K  L  L   I  Y  W

ACATCTACCC GGGAATCCGG GGTCCCTGCC CGATTCAGTG GCAGCGGGTC   200
T  S  T  R   E  S  G   V  P  A   R  F  S  G   S  G  S

TGGGACAGAT TTCACTCTCA CCATCAGCAG CCTGCAGGCT GAAGATGTGG   250
 G  T  D   F  T  L  T   I  S  S   L  Q  A   E  D  V  A

CAGTTTATTA CTGTCAGCAA TATTATAGTA CTCCACTCAC TTTCGGCGGA   300
  V  Y  Y   C  Q  Q   Y  Y  S  T   P  L  T   F  G  G

GGGACCATGG TGGAGATCAA GCGAACTGTG GCTGCACCAT CTGTCTTCAT   350
G  T  M  V   E  I  K   R  T  V   A  A  P  S   V  F  I

CTTCCCGCCA TCTGATGAGC CNGTNTGAAA TCTGGAACTG CCTCTGTTTG   400
 F  P  P   S  D  E  P   V  .  N   L  E  L   P  L  F  V

TGTGCCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACCAGTGGA   450
  C  P  A   E  .  L   L  S  Q  R   G  Q  S   T  S  G

AGGTGGATAA                                               460
R  W  I
```

D
J JH4b
Fig. 61


```
         10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
CNGCCTGTTA GGTCCNTGCG ACTCTCCTGT GCAGCGTCTG GATTCATCTT    50
X  P  V  R   S  X  R   L  S  C  A  A  S  G   F  I  F

CAGTAGNTAT GGCATGCACT GGGTCCGCCA GGCTCCAGGC AAGGGGCTGG   100
 S  X  Y   G  M  H  W   V  R  Q   A  P  G   K  G  L  E

AGTGGGTGGC AATTATATGG TATGATGGAA GTAATAAATA CTATGCAGAC   150
 W  V  A   I  I  W   Y  D  G  S   N  K  Y   Y  A  D

TCCGTGAAGG GCCGATTCAC CATCTCCAGA GACAATTCCA AGAACACGCT   200
S  V  K  G   R  F  T   I  S  R   D  N  S  K   N  T  L

GTATCTGCAA ATGAACAGCC TGAGAGCCGA GGACACGGCT GTGTATTACT   250
 Y  L  Q   M  N  S  L   R  A  E   D  T  A   V  Y  Y  C

GTGCGAGAGA CGGGGGGCCA CGGTGGTTTC TCGCTTCTGA CTACTGGGGC   300
 A  R  D   G  G  P   R  W  F  L   A  S  D   Y  W  G

CAGGGAACCC TGGTCACCGT CTCCTCAGCC TCCACCAAGG GCCCATCGGT   350
Q  G  T  L   V  T  V   S  S  A   S  T  K  G   P  S  V

CTTCCCCCTG GCGCCCTGCT CCAGGAGCAC CCTTCGAGAG CACAGCGGCC   400
 F  P  L   A  P  C  S   R  S  T   L  R  E   H  S  G  P

CTGGGCTGCC TGGTTCAAGG ACTACTTTCC CCGAACCGGT GACGGTGTNC   450
 G  L  P   G  S  R   T  T  F  P   E  P  V   T  V  X

GTTGGAACTC ATGAC                                         465
V  G  T  H   D
```

2/23/98

 JK- JK2 Fig. 62

```
        10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
AGTCTCCAGA CTCCCTGGTT GTGTCTCTGG GCGAGAGGGC CACCATCAAC     50
S  L  Q  T   P  W  L   C  L  W   A  R  G  P   P  S  T

TGCAAGTCCA GNCAGAGTAT TTTATACAGC TCCAACAATC AAAAACTTCT    100
 A  S  P   X  R  V  F   Y  T  A   P  T  I   K  N  F  L

TAGCTTGGTA CCAGCAGAAA CCAGGACAGC CTCCGAAGTT GCTCATTTAC    150
  A  W  Y   Q  Q  K   P  G  Q  P   P  K  L   L  I  Y

TGGGCATCTA TTCGGGAATC CGGGGTCCCT GACCGATTCA GTGGCAGCGG    200
W  A  S  I   R  E  S   G  V  P   D  R  F  S   G  S  G

GTCTGGGACA GATTTCACTC TCACCATCAG CAGCCTGCAG GCTGAAGATG    250
 S  G  T   D  F  T  L   T  I  S   S  L  Q   A  E  D  V

TGGCAGTTTA TTACTGTCAG CAGTATTATA GTATTCCGTG CACTTTTGGC    300
  A  V  Y   Y  C  Q   Q  Y  Y  S   I  P  C   T  F  G

CAGGGGACCA AGCTGGAGAT CAAACGAACT GTGGCTGCAC CATCTGTCTT    350
Q  G  T  K   L  E  I   K  R  T   V  A  A  P   S  V  F

CATCTTCCCG CCATCTGATG AGCAGTTGAA ATCTGGAACT GCCTCTGTTG    400
 I  F  P   P  S  D  E   Q  L  K   S  G  T   A  S  V  V

TGTGCCTGCT GAATAACTTC TATCCCAGAA AGGCCAAAGT ACATGAAGGG    450
  C  L  L   N  N  F   Y  P  R  K   A  K  V   H  E  G

TTCAAA                                                    456
F  K
```

V - DP50
D - D1R5
J - JH4b

63

Fig. 63

E20.11.2H Sequence

```
        10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
GGCGTGGYCC AGCCTGKGAG GTCCCTGAGA CTCTCCTGTG CAGCGTCTGG    50
G  V  X  Q   P  X  R   S  L  R   L  S  C  A   A  S  G

ATTCAYCTTC AGTARCTATG GCATGCACTG GGTCCGCCAG GCTCCAGGCA   100
 F  X  F   S  X  Y  G   M  H  W   V  R  Q   A  P  G  K

AGGGGCTGGA GTGGGTGGCA ATTATATGGT ATGATGGAAG TAGCAAATAC   150
  G  L  E   W  V  A   I  I  W  Y   D  G  S   S  K  Y

TATGCAGACT CCGTGAAGGG CCGATTCACC ATCTCCAGAG ACAATTCCAA   200
Y  A  D  S   V  K  G   R  F  T   I  S  R  D   N  S  K

GAACACGCTG TATCTGCAAA TGAACAGCCT GAGAGCCGAG GACACGGCTG   250
 N  T  L   Y  L  Q  M   N  S  L   R  A  E   D  T  A  V

TGTATTACTG TGCGAGAGAC GGGGGGCCAC GGTGGTTTCT CGCTTCTGAC   300
  Y  Y  C   A  R  D   G  G  P  R   W  F  L   A  S  D

TACTGGGGCC AGGGAACCCT GGTCACCGTC TCCTCAGCCT CCACCAAGGG   350
Y  W  G  Q   G  T  L   V  T  V   S  S  A  S   T  K  G

CCCATCGGTC TTCCCCCTGG CGCCCTGCTC CAGGAGCACC TTCCGAGAGC   400
 P  S  V   F  P  L  A   P  C  S   R  S  T   F  R  E  H

ACAGCGGCCC TGGGCTGCCT GGTCAAGGAC TACTTCCCCG AAMCGGTGAC   450
  S  G  P   G  L  P   G  Q  G  L   L  P  R   X  G  D

GGTGTCGTGG AACTCAGGCG CTCTGACCAG NGGCGTGCAC AATTCCCAGC   500
G  V  V  E   L  R  R   S  D  Q   X  R  A  Q   F  P  A

NGTCCTNAAG GTTGAAATCG TAANGGTTCA AA                      532
 V  L  K   V  E  I  V   X  V  Q
```

JKI

Fig. 64

```
          10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
ACTCAGTCTC CAGACTCCCT GGCTGTGTCT CTGGGCGAGA GGGCCACCAT    50
T  Q  S  P   D  S  L   A  V  S   L  G  E  R   A  T  I

CAACTGCAAG TCCAGCCAGA GTGTTTTATA CGGCTCCAAG AATCAGAACT   100
 N  C  K   S  S  Q  S   V  L  Y   G  S  K   N  Q  N  Y

ACTTAGCTTG GTACCAGCAG AAACCAGGAC AGCCTCCTAA GCTGCTCATT   150
  L  A  W   Y  Q  Q   K  P  G  Q   P  P  K   L  L  I

TACTGGGCAT CTACCCGGGA ATCCGGGGTC CCTGACCGAT TCAGGGGCAG   200
Y  W  A  S   T  R  E   S  G  V   P  D  R  F   R  G  S

CGGGTCTAGG ACAGATTTCA CTCTCACCAT CAGCAGCCTG CAGGCTGAAG   250
 G  S  R   T  D  F  T   L  T  I   S  S  L   Q  A  E  D

ATGTGGCAGT TTACTTCTGT CACCAATATT ATAGTACTCC GTGGACGTTC   300
  V  A  V   Y  F  C   H  Q  Y  Y   S  T  P   W  T  F

GGCCAAGGGA CCAAGGTGGA AATCAAACGA ACTGTGGCTG CACCATCTGT   350
G  Q  G  T   K  V  E   I  K  R   T  V  A  A   P  S  V

CTTCATCTTC CCGCCATCTG ATGAGCAGTT GAAATCTGGA ACTGCCTCTG   400
 F  I  F   P  P  S  D   E  Q  L   K  S  G   T  A  S  V

TTGTGTGCCT GCTGAATAAC TTGTATCCCA GAAAGCCAAG GACACGAAAG   450
  V  C  L   L  N  N   L  Y  P  R   K  P  R   T  R  K

GTCANACCNA CCC                                           463
V  X  P  T
```

2/23/98

D -
J- Fig. 65

E20.18MG30.Seq Sequence

```
         10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
CGTGATCCNC CTGGNTGGTC CCTGAGACTC TCCTGTGCAG CGTCTGGATT    50
R  D  P  P   G  W  S   L  R  L   S  C  A  A   S  G  F

CATCTTCANT AACTATTNCA TGCACTGGGT CCGCCAGGCT CCAGGCAAGG   100
 I  F  X   N  Y  X  M   H  W  V   R  Q  A   P  G  K  G

GGCTGGAGTG GGTGGCAATT ATATGGTATG ATGGAAGTAG CAAATACTAT   150
 L  E  W   V  A  I   I  W  Y  D   G  S  S   K  Y  Y

GCAGACTCCG NGAAGGGCCG ATTCACCATC TCCAGAGACA ATTCCAAGAA   200
A  D  S  X   K  G  R   F  T  I   S  R  D  N   S  K  N

CACGCTGTAT CTGCAAATGA ACAGCCTGAG AGCCGAGGAC ACGGCTGATG   250
 T  L  Y   L  Q  M  N   S  L  R   A  E  D   T  A  D  V

TATTACTGTG CGAGAGACGG TTGGGCCACG GTGGCTTCTC GCTTCTGACT   300
 L  L  C   E  R  R   L  G  H  G   G  F  S   L  L  T

ACTGGNGCNC AGGGCAACNC TGNCTNACCG TNTTCCTCAN CCCTNTACNC   350
T  G  A  Q   G  N  X   X  X  P   X  S  S  X   L  Y  X

AAGGGCCNCC ATTNGGTCTT TCCCCCCTGG NNNNCCTGCT CNATGNNNCA   400
 R  A  X   I  X  S  F   P  P  G   X  P  A   X  X  X  T

CCCTNCGACA NCNACAN                                       417
 L  R  X   X  X
```

J - JK2 Fig. 66

E20.18VK.Seq Sequence

```
        10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
TTCGTGGCTG TGTCTCTTGG CGAGAGGNCC ACCATCAACT GCAAGTCCAG    50
 F  V  A  V   S  L  G   E  R  X   T  I  N  C   K  S  S

CCAGAGTATT TTATACAGCT CCAACAATCA AAACTTCTTA GCTTGGTACC   100
  Q  S  I   L  Y  S  S   N  N  Q   N  F  L   A  W  Y  Q

AGCAGAAACC AGGACAGCCT CCGAAGTTGC TCATTTACTG GGCATCTATT   150
  Q  K  P   G  Q  P   P  K  L  L   I  Y  W   A  S  I

CGGGAATCCG GGGTCCCTGA CCGATTCAGT GGCAGCGGGT CTGGGACAGA   200
 R  E  S  G   V  P  D   R  F  S   G  S  G  S   G  T  D

TTTCACTCTC ACCATCAGCA GCCTGCAGGC TGAAGATGTG GCAGTTTATT   250
  F  T  L   T  I  S  S   L  Q  A   E  D  V   A  V  Y  Y

ACTGTCAGCA GTATTATAGT ATTCCGTGCA CTTTTGGCCA GGGGACCAAG   300
  C  Q  Q   Y  Y  S   I  P  C  T   F  G  Q   G  T  K

CTGGAGATCA AACGAACTGT GGCTGCACCA TCTGTCTTCA TCTTCCCGCC   350
 L  E  I  K   R  T  V   A  A  P   S  V  F  I   F  P  P

ATCTGATGAG CCAAGNTTGA AAATCTGGAA CTGCCTCTGT TGTGTGCCCT   400
  S  D  E   P  X  L  K   I  W  N   C  L  C   C  V  P  C

GCTTGAATAA CTTCTATCCC AGAGANGGCC AAAGTCCNGT GGAAGGTGGA   450
  L  N  N   F  Y  P   R  X  G  Q   S  P  V   E  G  G

TAC                                                      453
Y
```

E20.19.2MG30.Seq Sequence

J JH4b Fig. 67

```
          10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
CTCACCTGCA CTGTCTCTGG TGGCTCCATC AGTAGTTACT NTTGGAGNTG    50
L  T  C  T   V  S  G   G  S  I   S  S  Y  X   W  X  W

GATCCGGCAG CCCGNAGGGA AGGGACTGGA GTGGATTGGG TGTTTCTATT   100
 I  R  Q   P  X  G  K   G  L  E   W  I  G   C  F  Y  Y

ACAGNGGGAG CACCAACTAC AACCCCTCCC TNAAGAGTCA TGTCACCATA   150
 X  G  S   T  N  Y   N  P  S  L   K  S  H   V  T  I

TCAGTAGACA CGTCCAAGAA CCAGTTCTAC NTGAAGCTGA GCTNTGTGAC   200
S  V  D  T   S  K  N   Q  F  Y   X  K  L  S   X  V  T

CGNTGCGGAC ACGGNCGNGA ATAACTGNGC NAGAGATAGG GGAGNAGTGN   250
 X  A  D   T  X  X  N   N  X  A   R  D  R   G  X  V  X

NNTGGCNTNC TACTNTGACT ACTGAGGCCA GNGAACCNTG GNTCACAGTA   300
 W  X  X   T  X  T   T  E  A  X   E  P  W   X  T  V

ATCCNTAAGN CTNNCAANCA AANGNGNCCC AANGNGANAC NTNNCTNCNC   350
I  X  K  X   X  X  Q   X  X  P   X  X  X  X   X  X
```

JK- JK1

Fig. 68

E20.19.2VK.Seq Sequence

```
        10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
TCTTTGGTAG CGNGTCTTGG CGAGAGGCCC ACCATCAACT GCAAGTCCAG    50
S  L  V  A   X  L  G   E  R  P   T  I  N  C   K  S  S

CCAGAGTGTT TTATACNGCT CCAAGAATCA GAACTACTTA GCTTGGTACC   100
 Q  S  V   L  Y  X  S   K  N  Q   N  Y  L   A  W  Y  Q

AGCAGAAACC AGGACAGCCT CCTAAGCTGC TCATTTACTG GGCATCTACC   150
  Q  K  P   G  Q  P   P  K  L  L   I  Y  W   A  S  T

CGGGAATCCG GGGTCCCTGA CCGATTCAGG GGCAGCGGGT CTAGGACAGA   200
R  E  S  G   V  P  D   R  F  R   G  S  G  S   R  T  D

TTTCACTCTC ACCATCAGCA GCCTGCAGGC TGAAGATGTG GCAGTTTACT   250
 F  T  L   T  I  S  S   L  Q  A   E  D  V   A  V  Y  F

TCTGTCACCA ATATTATAGT ACTCCGTGGA CGTTCGGCCA AGGGACCAAG   300
  C  H  Q   Y  Y  S   T  P  W  T   F  G  Q   G  T  K

GTGGAAATCA AACGAACTGT GGCTGCACCA TCTGTCTTCA TCTTCCCGCC   350
V  E  I  K   R  T  V   A  A  P   S  V  F  I   F  P  P

ATCTGATGAG CACCTTGAAA TTCTGGAACT GCCTCTGNTG NGTGCCTGCT   400
 S  D  E   H  L  E  I   L  E  L   P  L  X   X  A  C  .

GAACNAACTC TATCCCCAGA GANGGCCCAA AAGTNTCAAG NNGGNNAGGC   450
  T  N  S   I  P  R   X  G  P  K   V  S  X   X  X  G

NNGATAACGC CTNTTCNCCN NCNTNC                             476
X  I  T  P   X  X  X   X
```

EGfr 20.21 Heavy

V- DP65
D DIR3
J- JH6b

69

Fig. 69

E20.20.21MG30.Seq Sequence

```
         10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
AAGCCTTTTC AGACCNTGCC CTTCACCTGC ACTGTCTCTG GTGGCTCCAT   50
K  P  F  Q   T  X  P   F  T  C   T  V  S  G   G  S  I

CAGCAGTGGT GGTTACTACT GGAGCTGGAT CCGCCAGCAC CCAGGGAAGG  100
 S  S  G   G  Y  Y  W   S  W  I   R  Q  H   P  G  K  G

GCCTGGAGTG GATTGGGTAC ATCTATAACA GTGGGAGCAC CTACTACAAC  150
 L  E  W   I  G  Y   I  Y  N  S   G  S  T   Y  Y  N

CCGTCCCTCC AGAGTCGAGT TACCATATCA GTAGACACGT CTAAGAACCA  200
P  S  L  Q   S  R  V   T  I  S   V  D  T  S   K  N  Q

GTTCTCCCTG AAGCTGAGCT CTGTGACTGC CGCGGACACG GCCGTGTATT  250
 F  S  L   K  L  S  S   V  T  A   A  D  T   A  V  Y  Y

ACTGTGCGGG TCAGAAATGG TCCTACTACT ACTACTACGG TATGGACGTC  300
 C  A  G   Q  K  W   S  Y  Y  Y   Y  Y  G   M  D  V

TGGGGCCAAG GGACCACGGT CACCGTCTCC TNAGCCTCCA CCAANGGCCC  350
W  G  Q  G   T  T  V   T  V  S   X  A  S  T   X  G  P

ATCGGTCTTC CCCCTGGCGC CCTGNTCTAG GAGCACCTCC CANAGCACAG  400
 S  V  F   P  L  A  P   X  S  R   S  T  S   X  S  T  D

ACGGATNCTG GGCCTGCCTG NATCAATGGA CTACTTTCCC CGAACCGGTT  450
 G  X  W   A  C  L   X  Q  W  T   T  F  P   E  P  V

GNNTGTGNNN CCTGGNAACT N                                 471
X  C  X  X   W  X  L
```

2/23/98

EGFr E20.22 Heavy

V- 4p118a11
D- D1R4
J- JH6b

70

E20.22MG30.Seq Sequence

Fig. 70

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
AAGCCTTTNG	AGACCNTGCC	CCTCACCTGC	ACTGTCTCTG	GTGGCTCCAT	50
K P X E	T X P	L T C	T V S G	G S I	
CAGTAATTAC	TACTGGAGCT	GGATCCGGCA	GCCCCCAGGG	AAGGGACTGG	100
S N Y	Y W S W	I R Q	P P G	K G L E	
AGTGGATTGG	GTATATCTAT	TACAGTGGGA	GCACCAACTA	CAACCCCTCC	150
W I G	Y I Y	Y S G S	T N Y	N P S	
CTCAAGAGTC	GAGTCACCAT	ATCAGTAGAC	ACGTCCAAGA	ACCAGTTCTC	200
L K S R	V T I	S V D	T S K N	Q F S	
CCTGAAGCTG	AGCTCTGTGA	CCGCTGCGGA	CACGGCCGTG	TATTACTGTG	250
L K L	S S V T	A A D	T A V	Y Y C A	
CGAGAGGGCC	CGGGGGGAGC	TACTACTACT	ACGGTATGGA	CGTCTGGGGC	300
R G P	G G , S	Y Y Y Y	G M D	V W G	
CAAGGGACCA	CGGTCACCGT	CTCCTCAGCC	TCCACCAAGG	GCCCATCGGT	350
Q G T T	V T V	S S A	S T K G	P S V	
CTTCCCCCTG	GCGCCCTGCT	CCAGGAGCAC	CTCCGAGAGC	ACAGCGGCCC	400
F P L	A P C S	R S T	S E S	T A A L	
TGGGCTGCCT	GGGTCAAGGA	CTACTTCCCC	GAACCGGTGA	CGGTGTTCGN	450
G C L	G Q G	L L P R	T G D	G V R	
NGGAAC					456
X N					

Amino Acid Sequences and Structure of Human Heavy Chain Derived from EGFR-Specific Hybridomas

```
Human γ2          CDR1                   CDR2                                                  CDR3
4-31      VSGGSISSGGYYWSWIRQHPGKGLEWIGYIYYSGSTYYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR                                    ASTKGPSVFPPLAPCSRSTST
[illegible].1      ------N--D--------------DC----------------------------------F---T--------------STVVNPG  WFDP   WGQGTLVTVSS  -------------------
E2.4      ------N--D------------------S-----N-F---------L--------------------------C----NIVTTG   AFDI   WGQGTMVTVSS  -------------------
E2.5      ---------D---T-----------------------N----------SM-I---E--------------------------KPVTGG   EDY    WGQGTLVTVSS  -------------------
E6.2      ------N--DF---------------------------------------M-I-P---------I---------------TSLYYGG  GMDV   WGQGTTVTVSS  -------------------
E6.4      ------NN-D------------------H---------I------T---------------N-----------------GTVTTYY  YFDY   WGQGTTVTVSS  -------------------
E20.21    ---------C------------------------N---------Q-----------------------------------GKWSYYYYYGMDV  WGQGTTVTVSS  -------------------

                  CDR1                   CDR2                                                  CDR3
4-61      VSGGSVSSGSYYWSWIRQPPGKGLEWIGYIYYSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAR
E2.11     ---------D------------------HL----N------------L--------------------------------DFLTGSF  FDY    WGQGTMVTVSS  -------------------
E6.3      ------Y--D----------------------------------------------------------------------DSILGA   TNY    WGQGTLVTVSS  -------------------
E7.6.3    ---------D---T----S---------H-----N--------L---I----T------------I---V-DRVTGA   FDI    WGQGTMVTVSS  -------------------
```

09187692 . 110699

Figure 71

Figure 72

E7.5.2.K.aa Sequence

```
         10         20         30         40         50
1234567890 1234567890 1234567890 1234567890 1234567890
CTGTCTGCAT CTGTAGGAGA CAGAGTCATA ATCACTTGCC GGGCAAGTCA     50
L  S  A  S   V  G  D   R  V  I   I  T  C  R   A  S  Q

AAACATCACC GACCATTTAA ATTGGTATCA GCAGATAGCA GGAAAAGCCC    100
 N  I  T   D  H  L  N   W  Y  Q   Q  I  A   G  K  A  P

CTAGGCCCCT GATATACACT GCATCCAGTT TGCAAGGTGG GGTCCCATCA    150
  R  P  L   I  Y  T   A  S  S  L   Q  G  G   V  P  S

AGGTTCAGTG GCAGTGGATC TGGGACAGAT TTCACTCTCA CCATCAGCAG    200
R  F  S  G   S  G  S   G  T  D   F  T  L  T   I  S  S

TCTGCAACCT GAAGATTTTT CAACTTACTA CTGTCAACAG AGTTACAGTA    250
 L  Q  P   E  D  F  S   T  Y  Y   C  Q  Q   S  Y  S  T

CCCCGTGCAG TTTTGGCCAG GGGACCAAGC TGGAGATCAA ACGAACTGTG    300
  P  C  S   F  G  Q   G  T  K  L   E  I  K   R  T  V

GCTGCACCAT CTGTCTTCAT CTTCCCGCCA TCTGATGAGC AGTTGAAATC    350
A  A  P  S   V  F  I   F  P  P   S  D  E  Q   L  K  S

TGGAACTGCC TCTGTTGTGT GCCTGCTGAA TAACTTCTAT CCCA          394
 G  T  A   S  V  V  C   L  L  N   N  F  Y   P
```

E7.5.2.v.aa Sequence

Figure 7з

10	20	30	40	50	
1234567890	1234567890	1234567890	1234567890	1234567890	
GTGAAGGTCT	CCTGCAAGGC	TTCTGGATAC	ACCTTCAGCG	GCTACTATAT	50
V K V S	C K A	S G Y	T F S G	Y Y M	
GCACTGGGTG	CGACAGGCCC	CTGGACAAGG	GCTTGAGTGG	ATGGGATCGA	100
H W V	R Q A P	G Q G	L E W	M G S I	
TCCACCCTAA	CAGTGGTGGC	ANAAACTTTG	CACAGAAGTT	TCAGGGCAGG	150
H P N	S G G	X N F A	Q K F	Q G R	
GTCACCATGA	CCAGGGACAC	GTCCATCAAC	ACAGCCTACT	TGGAGCTGAG	200
V T M T	R D T	S I N	T A Y L	E L S	
CAGGCTGAGA	TCTGACGACA	CGGCCGTGTA	TTACTGTGCG	AGAGATAAAA	250
R L R	S D D T	A V Y	Y C A	R D K N	
ACTACGGTGA	CTACGTCTTT	GACTATTGGG	GCCAGGGAAC	CCTGGTCACC	300
Y G D	Y V F	D Y W G	Q G T	L V T	
GTCTCCTCAG					310
V S S					

09845111 0011

Figure 74 Effect of E7.6.3 or E7.5.2 on human epidermoid carcinoma A431 growth in nude mice

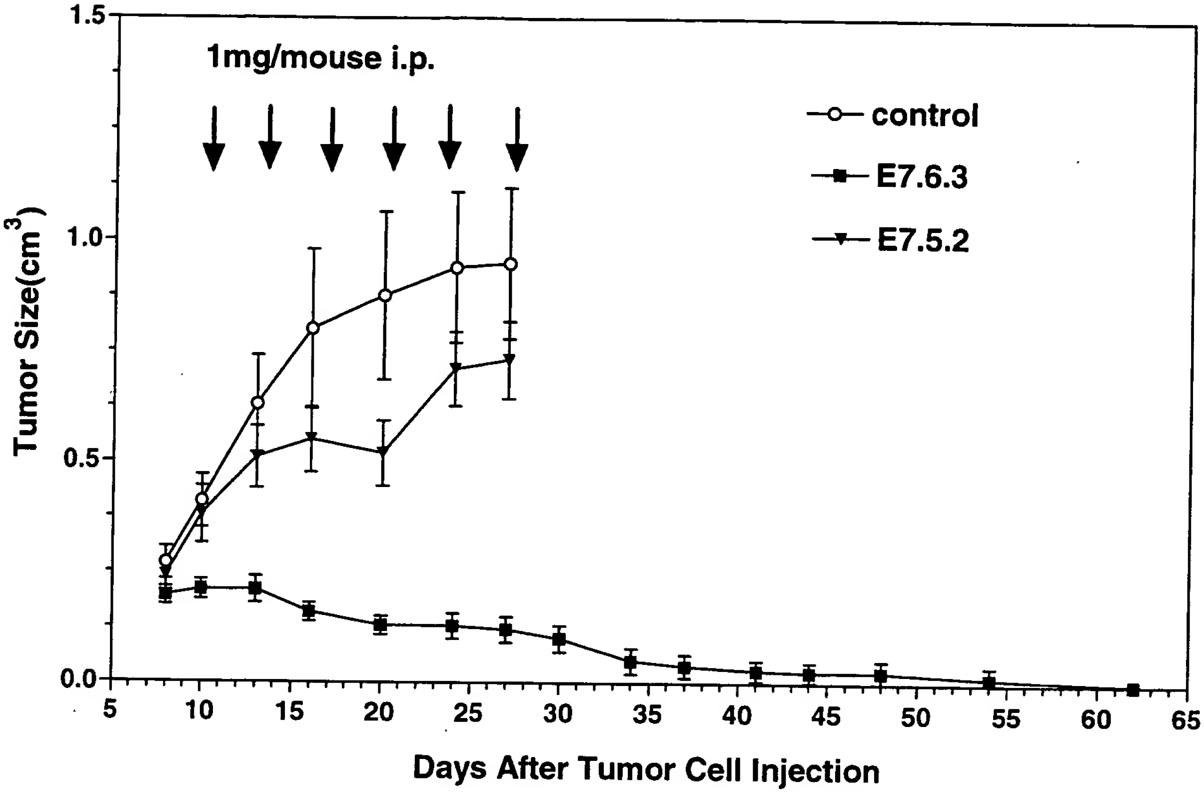
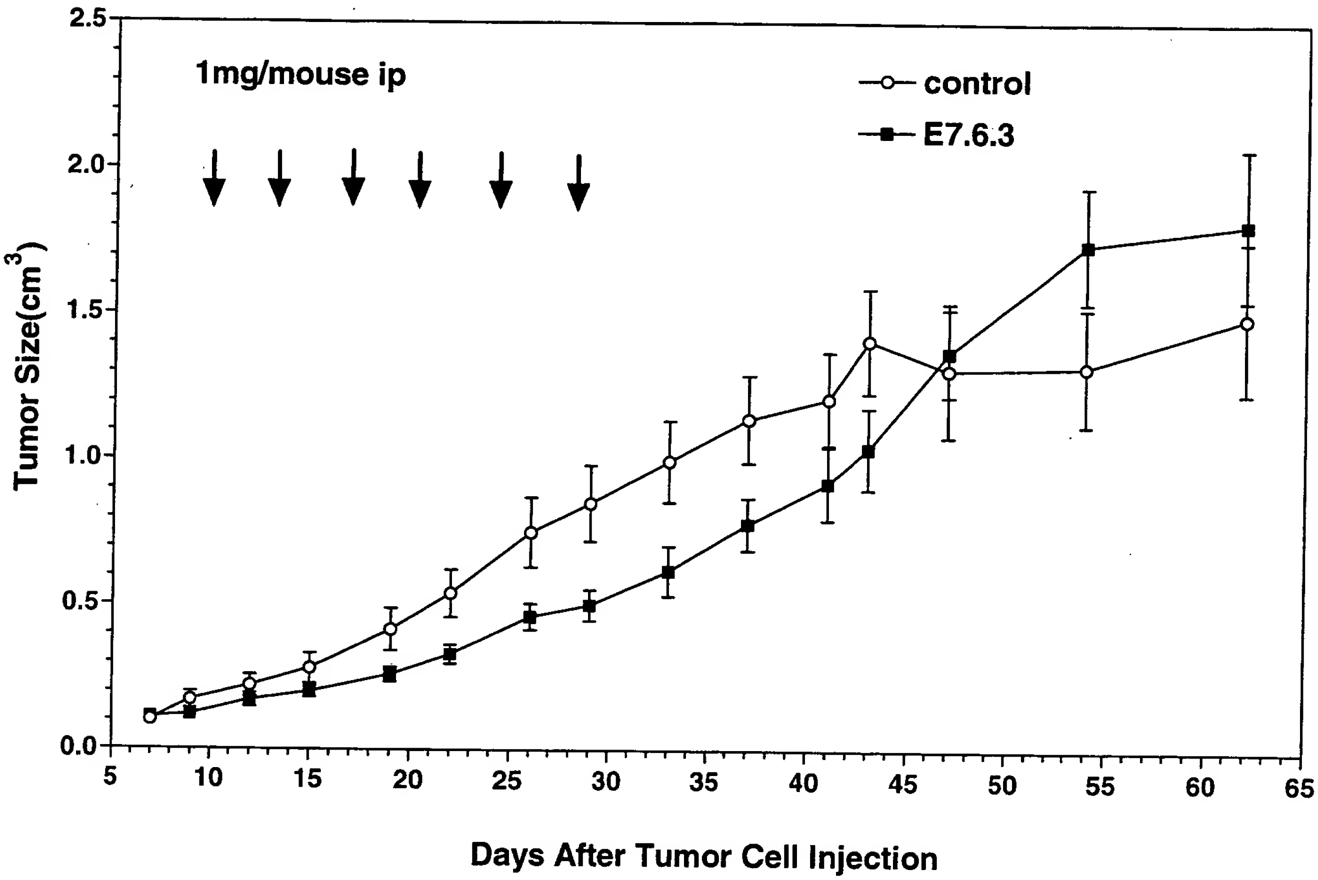


Figure ~~8~~ 75. Effect of E7.6.3 on human pancreatic carcinoma HPAC growth in nude mice



09507153.027600

FIGC-E~1.PZM:Graph-1 - Thu Nov 05 11:46:00 1998

Figure ~~6~~ 76 Effect of E7.6.3 on human pancreatic carcinoma BxPC-3 growth in nude mice

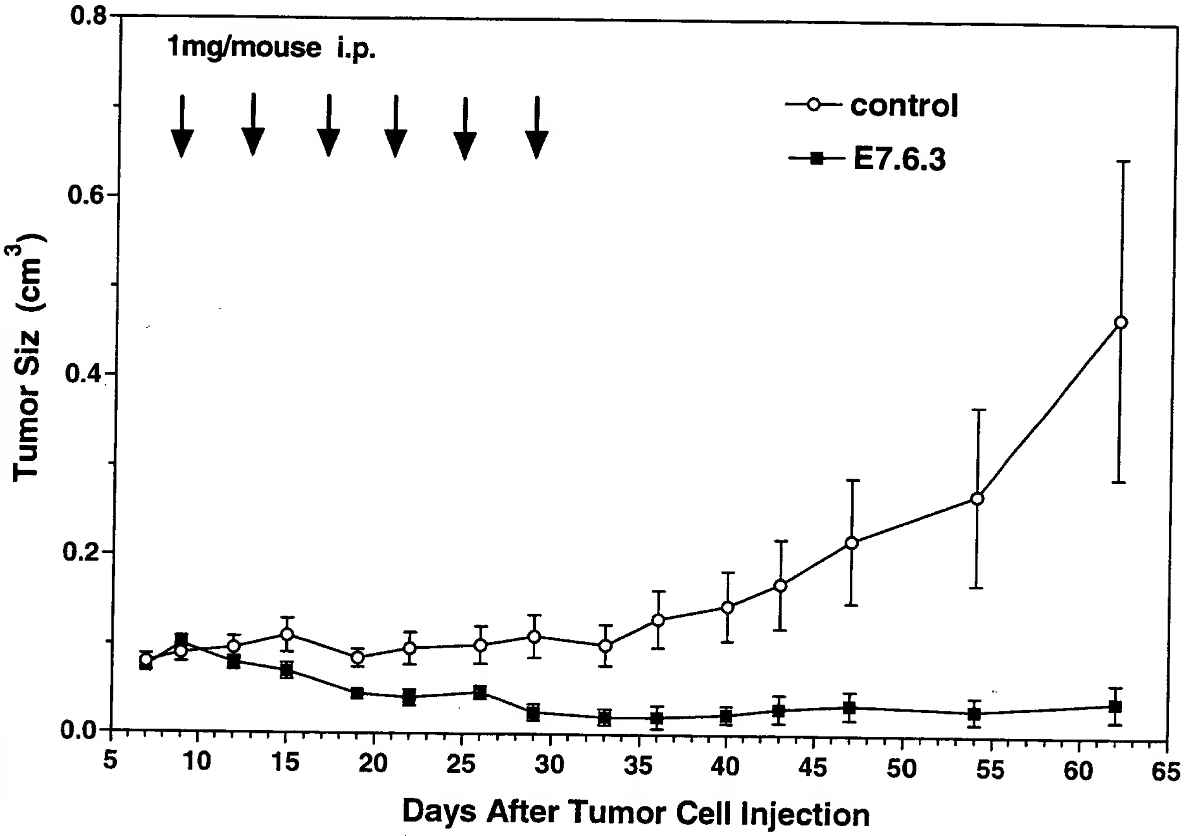


Figure ~~B~~ 77. Effect of E7.6.3 on HS766T Pancreatic tumor growth in nude mice

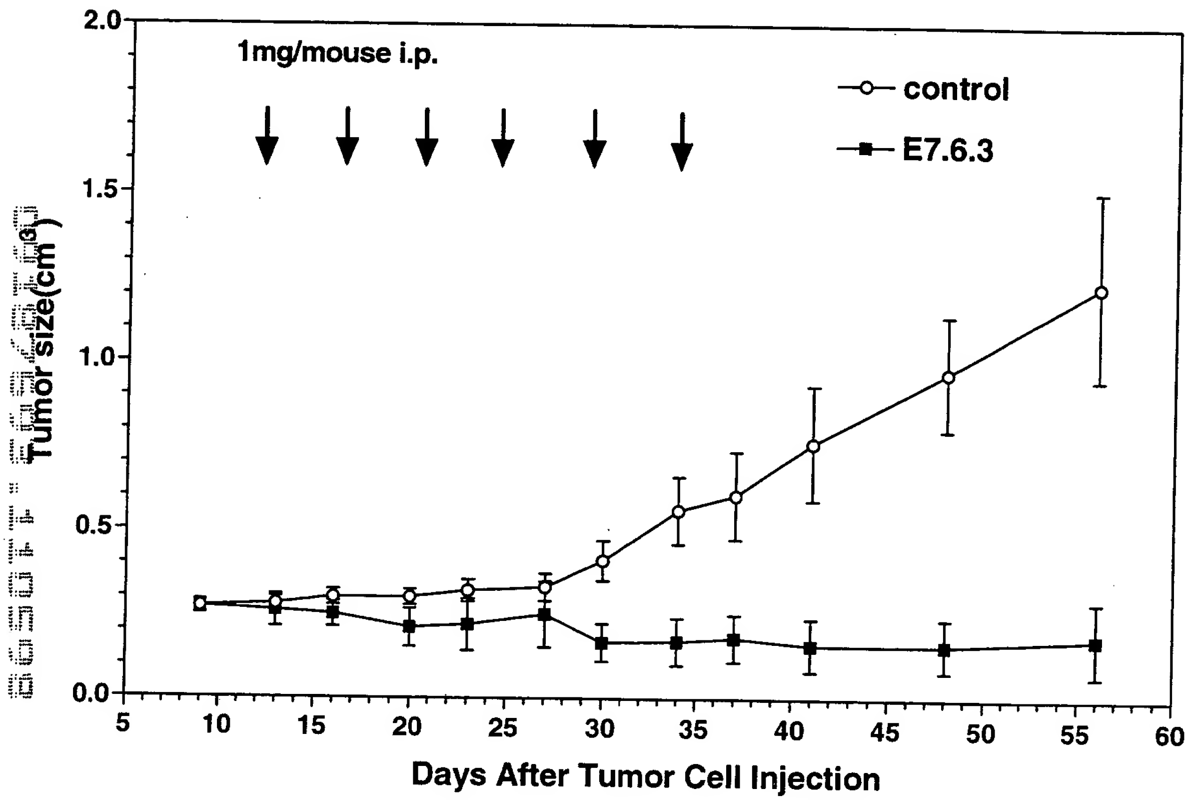
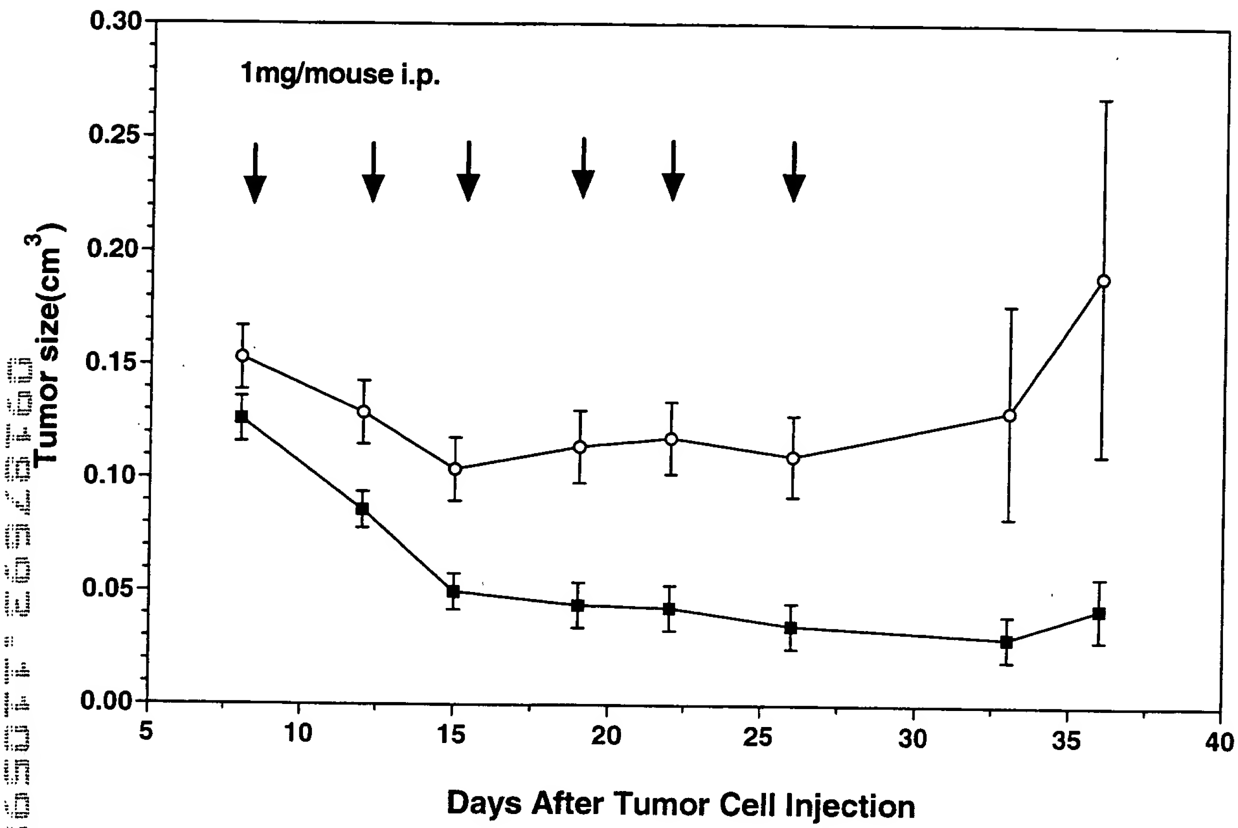


Figure ~~E~~ 28. Effect of E7.6.3 on SK-RC-29 human kidney carcinoma growth in nude mice

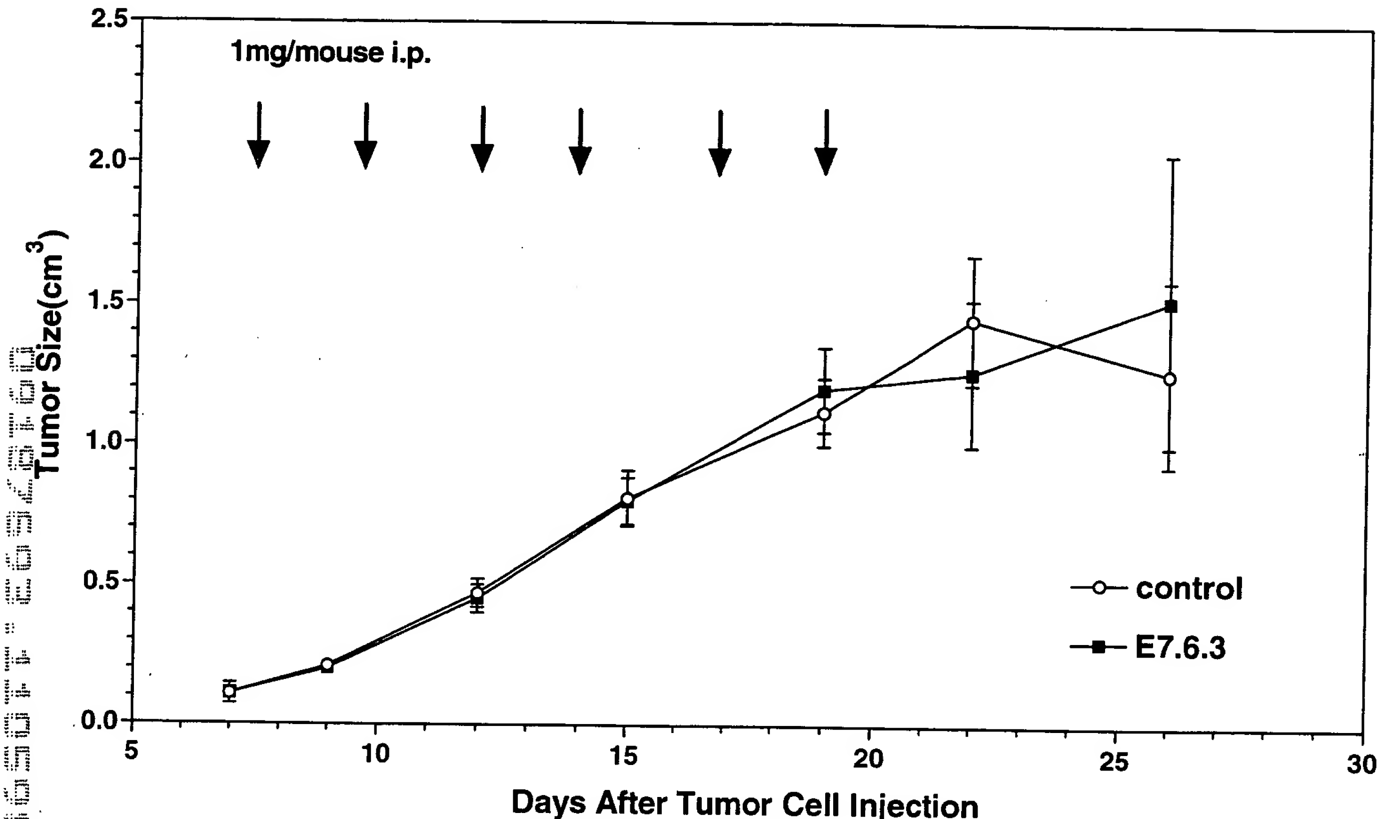


—o— control no treatment

—■— E7.6.3 neutralizing mAb

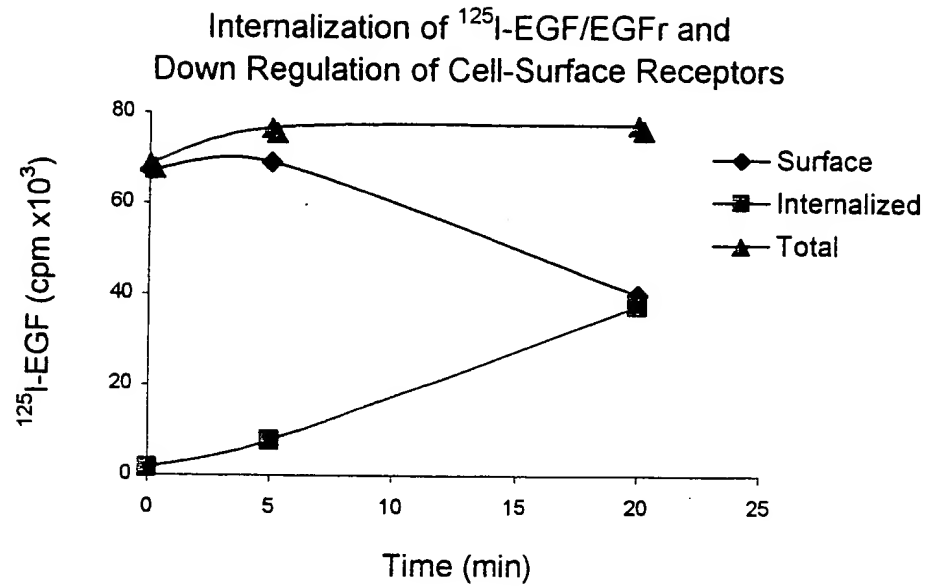
09507163.110598

Figure ~~8~~ 79 Effect of E7.6.3 on human colon carcinoma SW707 (EGFr−) growth in nude mice



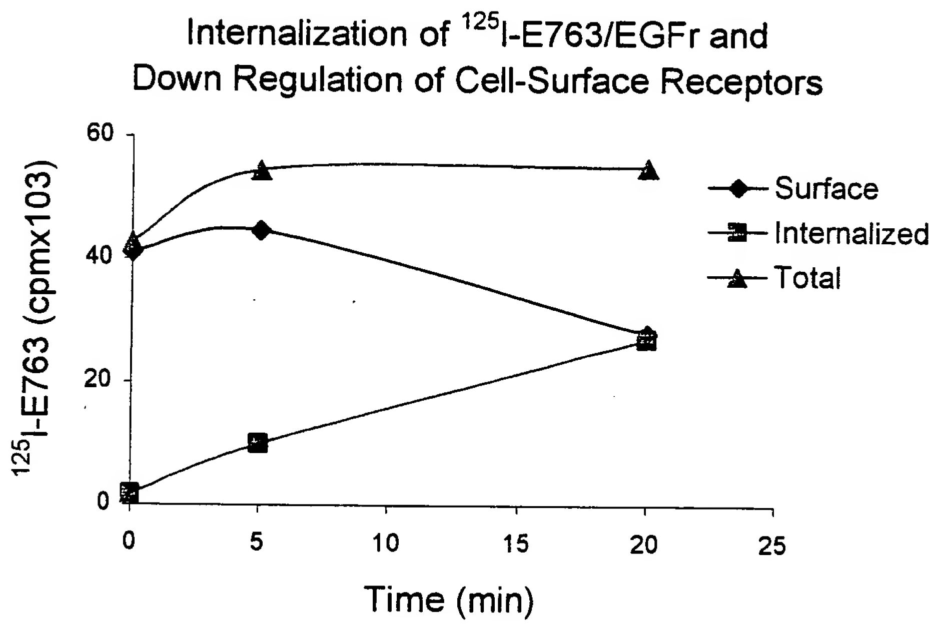
09581593 . 111598

Figure 80



A

^{125}I-EGF	Time (min	Surface	Internalize	Total	% internalized
	0	67.153	1.515	68.668	2.2
	5	68.997	7.649	76.646	10
	20	39.986	37.406	77.392	48



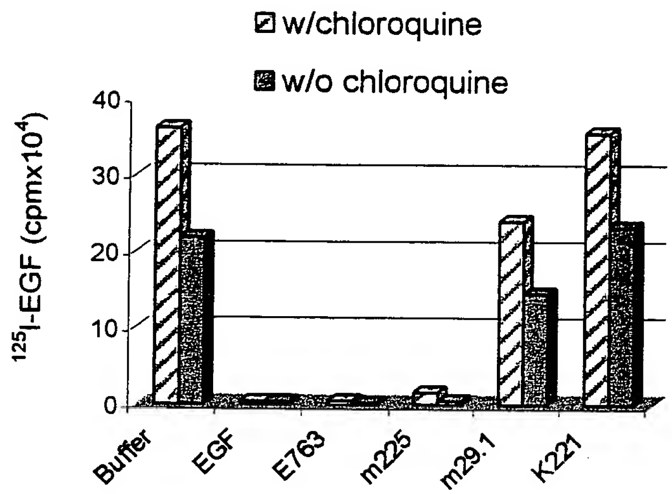
B

^{125}I-E763	Time (min	Surface	Internalize	Total	% internalized
	0	41.051	1.684	42.735	3.9
	5	44.567	9.876	54.443	18
	20	27.969	26.998	54.967	49

8/25/98, 110-40, Jia

Figure 81

Degradation of ^{125}I-EGF or ^{125}I-E763 after binding to EGFr on A431 cell

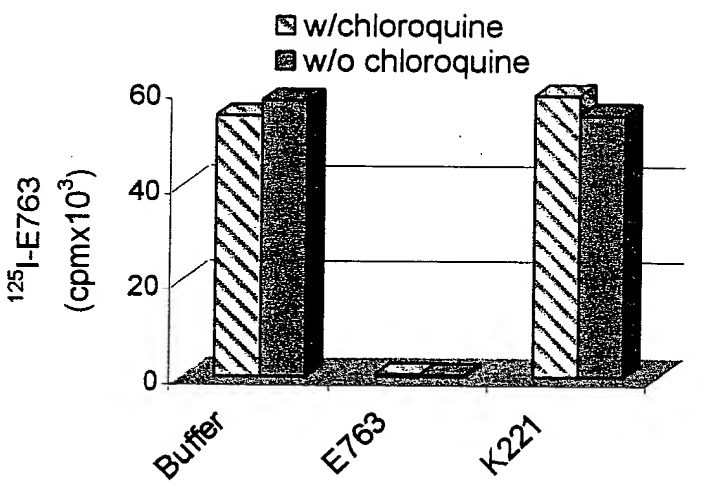


^{125}I-EGF

A

w/ or w/o chloroquine (100μM)

		w/chloroq	w/o chloroquine	% degradation	% competition
cpmx10^4	Buffer	36.0898	21.8277	40	0
	EGF	0.3684	0.3776		98
	E763	0.481	0.2132		99
	m225	1.5468	0.4882		98
	m29.1	23.9704	14.459		34
	K221	35.5084	23.2694	34	1.6



^{125}I-E763

B

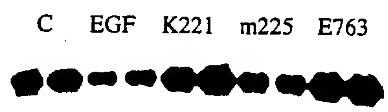
w/ or w/o chloroquine (100μM)

		w/chloroq	w/o chloroquine	% degradation	% competition
cpmx10^4	Buffer	54.608	57.824	0	0
	E763	0.536	0.441		99
	K221	58.956	54.83	7	5

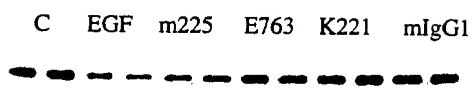
8/25/98, 110-46, Jia

Figure 82

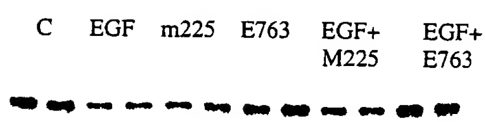
Effects of E763 and m225 on EGFr degradation



A



B



C

Figure 83

Effects of E763 and m225 on EGFr threonine phosphorylation

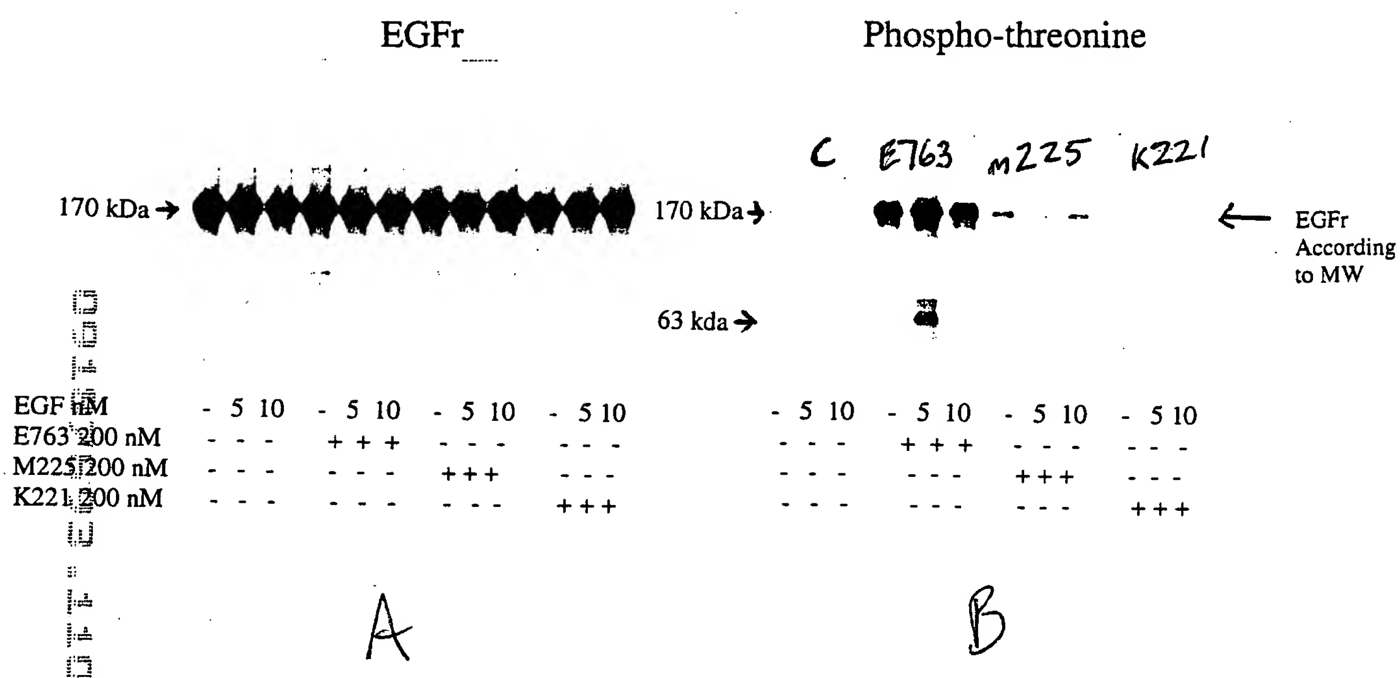


Figure 84

tyr. phos. protocol

thr-phos detect

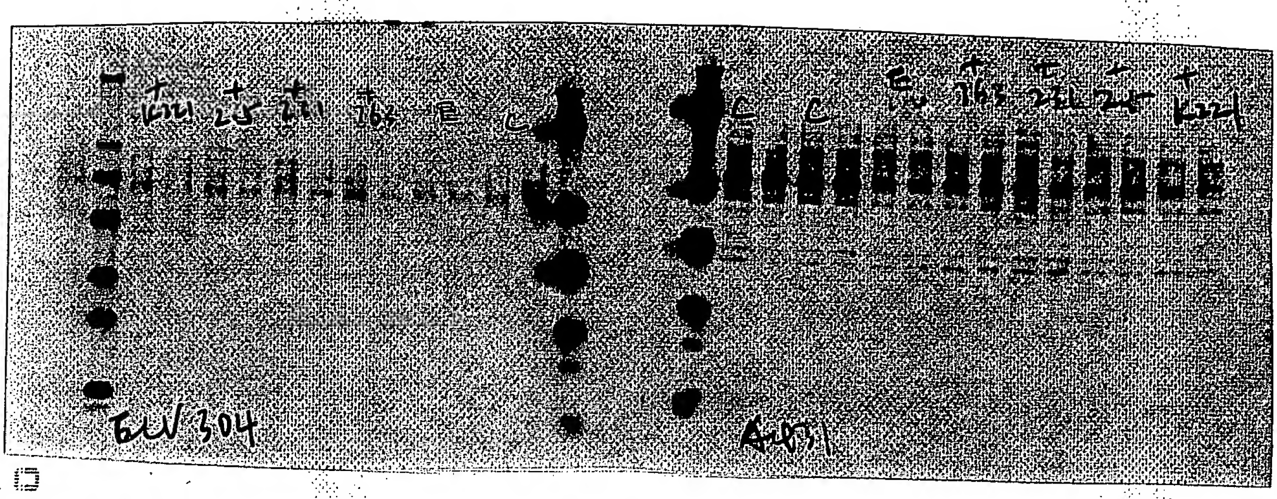
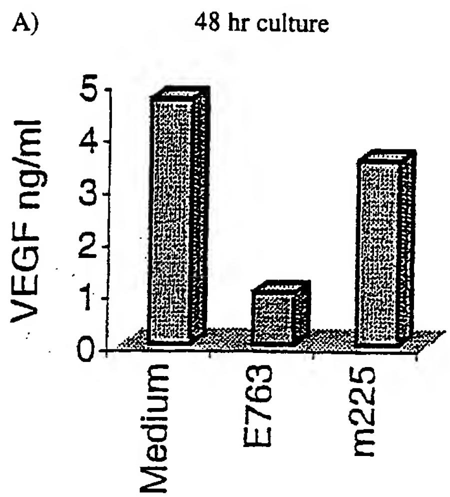


Figure 85

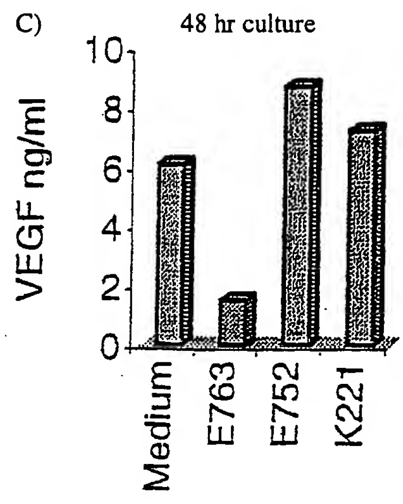
E763 on VEGF secretion

Effects of E763 and m225 on
VEGF secretion
in cultured A431 cells



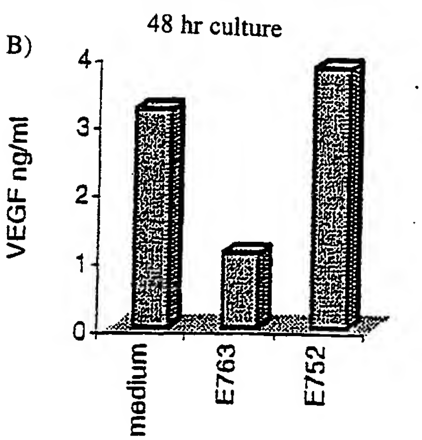
A

Effects of E763 and E752 on
VEGF secretion
in cutured A431 cells



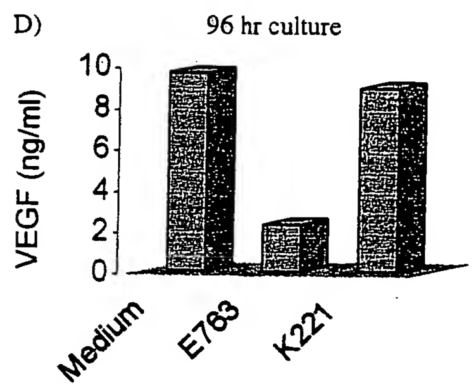
B

Effects of E763 and E752 on
VEGF secretion
in cultured A431 cells (24 hr)



C

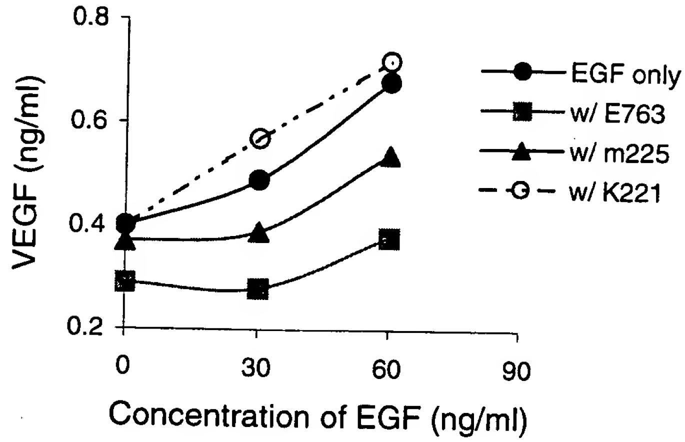
Effect of E763 on VEGF secretion in
cultured A431 cells



D

Figure 86

Effects of E763 and m225 on VEGF secretion in cultured endothelial cells



11/5/98 VEGF in endothelial cells (ECV304) (ATCC ; CRL-1998)

VEGF ng/ml		no serum	
	0	30	60
EGF only	0.4	0.49	0.68
w/ E763	0.29	0.28	0.38
w/ m225	0.37	0.39	0.54
w/ K221	0.4	0.57	0.72